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Risk Factors for Clinical Typhoid Fever in Villages in Rural South-Sulawesi, Indonesia

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Abstract: A survey was carried out among all household heads in five neighbouring villages in rural South-Sulawesi, Indonesia, to collect information on the prevalence of typhoid fever and of demographic and behavioural risk factors for having typhoid. The household heads recalled 134 cases of typhoid fever during the preceding year of whom 90% had been diagnosed based on clinical findings by a trained health worker. The following independent risk factors were identified: consumption of uncooked vegetables (aOR, 5.31), consumption of water with a poor quality (aOR, 5.29), use of water that is contaminated with coliform bacteria (aOR, 4.11), not washing hands before eating (aOR, 9.73) and not using soap for washing hands (aOR, 2.84). The results indicate that in the absence of clean drinking water and adequate sanitation education focussing on simple measures such as hand washing with soap before eating and cooking of vegetables before consumption may contribute to the prevention of typhoid fever in rural areas.

Key words: Typhoid fever, risk factors, education, living conditions, hygiene, sanitation, behaviour, water quality, foot habits, vaccination, environment

INTRODUCTION

Typhoid still is a major public health issue in many tropical countries in particular in Southeast Asia (Pang *et al*., 1998; Parry *et al*., 2002). This potentially severe disease is endemic in Indonesia and is reported to be the fourth most prevalent infectious disease in most of South-Sulawesi. Typhoid fever is primarily but not exclusively caused by infection with *Salmonella enterica* subsp. enterica serovar Typhi. In contrast to other parts of Asia, where multi-drug-resistant serovar Typhi is common and has led to large epidemics, multi-drug-resistant serovar Typhi has not been reported from Indonesia and in this country chloramphenicol still is highly effective as the first line drug. Morbidity and mortality nevertheless are high in particular among hospitalized patients. Self-medication and consultation of medical staff at a late stage likely contribute to disease severity and the occurrence of complications in some patients.

Humans are the only natural hosts and reservoirs and transmission is caused by ingestion of food or water that is contaminated with fecal excretions or urine from carriers or ex-patients. Sanitation, health education and vaccination are main tools for the control of typhoid. However, the weak economic position of communities in areas where typhoid is endemic poses severe restrictions on any health programme. The identification of specific risk factors could well help to develop and prioritize public health policies such that the scarcely available resources can be used most effectively.

In areas that are relatively free of typhoid, outbreaks usually occur from a single source of food or carrier (Birkhead *et al*., 1993; Gruner *et al*., 1997). Safe drinking water supplies are of prime importance in controlling typhoid as is exemplified by a massive outbreak in Tajikistan due to sewage contaminated drinking water after breakdown of the city water supply system (Mermin *et al*., 1999). In endemic areas with poor sanitation and hygiene and a weak infrastructure the situation may be entirely different with continuous exposure of the whole population from multiple sources. Epidemiological studies performed in endemic areas have pointed to a variety of risk factors. One study conducted in an urban area on Java, Indonesia showed that low socio-economic status, poor housing with inadequate water supply and open sewers and inappropriate personal hygiene were associated with an increased risk of getting typhoid (Gasem *et al*., 2001). Another study performed in Indonesia in an urban community endemic for enteric

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fever in Jakarta, the capital of Indonesia, showed that risk factors for typhoid fever were a recent typhoid fever case in the household, not using soap for hand washing, sharing food from the same plate and absence of a toilet in the household (Vollaard *et al*., 2005). Other studies conducted in cities in Indonesia, Chile and Pakistan reported that eating and drinking outside the home were risk factors (Velema *et al*., 1997; Black *et al*., 1985; Luby *et al*., 1998) and a study performed in the Philippines indicated that street vendors play an important role in transmission (Castillo *et al*., 1995). This seemingly contrast with the study performed by Vollaard *et al*. (2005), which demonstrated that risk factors for typhoid fever are generally related to factors within the household whereas risk factors related to paratyphoid are determined by conditions outside the household.

Studies performed in Chile indicated that secondary cases are rare that chronic carriers within the household do not play an important role and showed that consumption of sewage contaminated raw vegetables was the key factor in outbreaks in that country (Morris *et al*., 1984; Black *et al*., 1985). However, recent contact with a typhoid patient was the most important risk factor in a recent hospital based study conducted in the Mekong delta in Vietnam (Luxemburger *et al*., 2001). Recent contact with a typhoid patient, the consumption of contaminated water and lack of education were found to be the major risk factors in another study performed in Northern Vietnam (Tran *et al*., 2005). In addition, human factors including major histocompatibility gene subclasses and tumor necrosis factor are involved as well and certain haplotype may provide protection to infection (Dunstan *et al*., 2001a, b; 2007). Finally, one study has pointed to the association between *Helicobacter pylori* infection and increased risk for typhoid (Bhan *et al*., 2002).

Risk factors in endemic areas may differ between areas depending on the degree of development, education, sanitation and hygiene and the availability and quality of drinking water. In Indonesia, South-Sulawesi probably has the highest number of reported cases in the country. Numbers exceed 5,000/100,000 annually (South-Sulawesi health department reports). Cases occur throughout the year but may peak during the dry season. We conducted a village survey in a rural community in the Jeneponto Sub-district in South-Sulawesi to identify risk factors for typhoid.

MATERIALS AND METHODS

Study area: The study was performed in the 5 villages of the Jeneponto Sub-district in South-Sulawesi, Indonesia. The Jeneponto Sub-district is a remote undeveloped area situated 146 km South of Makassar, the provincial capital. The Sub-district consists of five neighbouring villages, Bonto Lebang, Rannaya, Ta'Bassi, Panrang-Panrang and Ta'Lambua. The area is hilly with Bonto Lebang, Rannaya and Ta'Bassi located on hilltops, Panrang-Panrang on a slope and Ta'Lambua at the bank of a small river. The population is composed mainly of farmers with most of them living in small one-story houses build on poles and lined along the dirt roads.

People living in the area almost entirely depend on locally produced staple food and crops for their nutritional needs. The main staple food is corn. Most households keep some livestock at their compound. The mother with the help of children generally prepares food and consumption of food prepared and purchased elsewhere is very exceptional. Food stalls or other places to eat or to drink do not exist in the area. The villages depend for their water supplies almost entirely on open sources including several wells scattered throughout the villages, the river, some small ponds and a narrow irrigation canal running along the road to Jeneponto. Only a few wells are closed. Neither piped nor bottled water is available in the area. The rainy season is from early December to mid May but often shorter. During the dry season, most of the wells in villages on the hills become dry. During the rainy season, open wells may flood and become contaminated with surface water.

Typhoid, locally also called garing lelleng because the traditionally used herbal medication causes a blackening of the skin is well known among the local population and in cases of a persisting febrile illness most patients will seek medical attention. A medical doctor and the primary health care center in Jeneponto and a nurse and a midwife both living in Rannaya provide medical care. The staff of the health care center and the nurse and midwife have been trained to recognize and treat the major infectious diseases. Diagnosis is based on clinical findings exclusively. Typhoid fever is diagnosed in patients with fever for 1 week and if one or more of the following symptoms are present: malaise, rigors, severe headache, nausea, abdominal pain, constipation, rose spots and a coated tongue. Other presentations sometimes seen are hepatomegaly, splenomegaly, bradycardia and apathy or coma. Severe cases are referred to the district hospital in Jeneponto city or directly to one of the hospitals in Makassar.

Study design: We conducted a retrospective cross-sectional village survey. The survey was conducted in September, 2002 at the end of the dry season. For data collection a medical doctor from the Hasanaddin Medical University instructed a survey team consisting of staff from the department of communicable diseases control of

the province of South-Sulawesi and of staff from sub-district disease surveillance team. During a period of 2 weeks, members of the team visited all 365 households at their home and interviewed the household heads. The aim of the study was explained and the questions were put using a structured questionnaire. Household heads were asked to recall any illness including typhoid occurring in their household during the 12 months period preceding the interview. The medical data were checked with the local health workers. In addition, the questionnaire inquired about demographic data, education and health status and collected data per household on travel, socio-economic markers, living conditions, water supplies, sanitation, food consumption and preparation and hygienic behaviour.

Laboratory testing: At all households a laboratory worker from the department of medical microbiology of the Hasanuddin University collected water samples from storage containers for drinking water supplies for bacteriological examination for the presence of coliform bacteria. In households, where water for drinking was generally boiled water was collected from containers containing boiled water and the quality was compared with a sample from their preferred water source. The effect of boiling on the bacteriological quality of water was determined by examination of boiled and unboiled samples collected from all households. Households that normally did not boil their drinking water received specific instructions for boiling. Water samples were collected in 250 mL sterile bottles. To test for the presence of coliform contaminants 0.1, 1.0 and 10 mL quantities were cultured in Durham bottles containing bile salt lactose peptone medium. Samples were considered positive when at least one out of 5 cultures inoculated with 10 mL water was found positive. The laboratory worker also examined the quality of the water by rating the odour, colour and taste.

Statistical analysis: Statistical analysis was done using the Epi-Info 6.0 and SPSS 11.0 software to determine, which household and behavioural characteristics were associated with an increased risk for having typhoid fever. Risk factors were first identified by univariate analysis. Variables that contained >2 categories were grouped into fewer categories by combining categories showing an identical risk. A multivariate logistic regression analysis was then performed to identify which of the potential risk factors (i.e., with $p<0.15$) remained independently associated with typhoid.

Ethical approval: Permission for the study was obtained from the ethical committee of the Hasanuddin University, the village leaders and household heads.

RESULTS

The demographic characteristics of the households from the 5 neighbouring villages are shown in Table 1. In 2002, the population of the villages consisted of 1957 inhabitants in 365 households. The average household income/year amounted to the equivalent of US$ 22 only for a mean of 4.6 individuals/household. Illiteracy is relatively high. In the age group above 18 years (n = 1175) 58.4% of the individuals had attended primary school, 4.2% had completed secondary school, 1.8% had received a higher level of education and 36.6% had received no formal education. The level of formal education among males and females was the same except that more females (n = 19) than males (n = 6) had an education level higher than secondary school. The quality of houses generally is poor. Better quality houses differed from moderate and poor quality houses in that they more often had a ceramic or cement floor instead of one made of wood, bamboo or sand, more often had walls made of stone or wood than made of bamboo and more often had roofs made of wood, tiles or zinc than made of sedge or sago palm. Locally produced corn is the main staple food. The diet is supplemented with some rice and some vegetables such as amaranth, cabbages and tomatoes.

Most (93.1%) households obtain water for consumption from an open source being either a well, pond, river or the irrigation canal. However, households may obtain their water from different sources at different periods during the season depending on water levels. The median distance to the water source was 100 m. The distance varies between the villages (median distance, 43-200 m) and households (1-1000 m). Relatively few households (11.2%) have access to a toilet emptying in a closed pit. Demographic differences between the villages were not found except that households of the two villages located farthest away from the river more frequently use their garden for disposal of human excretions and more often obtained water from wells for bathing while households of the other three villages used the river or a pond for these aims.

Typhoid was found to be the most important health problem with 134 cases recalled by household heads for the past year (Table 2). Diarrhoeal disease (n = 83) and influenza-like illness (n = 71) were the next most frequently recalled diseases. In total 109 (29.9%) households had one or more patients with typhoid in the period of investigation; 85 households had one patient with typhoid, 23 households had two patients and one had three patients. The prevalence of clinical typhoid was calculated to be 6,847/100,000/year. The inhabitants of the 5 villages were affected equally ($p = 0.99$). For medical attention patients most often went to the primary health

Table 1: Demographic characteristics of the five neighbouring villages of the Jeneponto Sub-district in 2001

Variables	No. or value (ratio, range or percent)
No. of houses	365
No. of population	1957
No. of male/female (ratio)	959/998 (0.96)
Mean age in years (range)	25.1 (0-78)
No. of persons/household (range)	5.4 (1-15)
Marital status (married /not married)	886/1071
Education	
None	758 (38.7)
Primary school only	1104 (56.5)
Secondary school	69 (3.5)
Higher education	25 (1.3)
Mean income	227.000 rupia (25-75%, 190.000-275.000)
Quality of the house	
Poor	202 (55.3)
Fair	141 (38.7)
Good	22 (6.0)
Source of drinking water	
Closed well	25 (6.8)
Open well/river/pond	340 (93.2)
Latrine type	
Private or public toilet	41 (11.2)
Pond or river	120 (32.9)
Garden	178 (48.8)
Open sewer	26 (7.1)
Place used for bathing	
Private well	43 (11.7)
Public well	234 (64.1)
Pond, river or canal	84 (23.0)
Water storage	4 (1.1)
Place of medical care	
Medical doctor	7 (1.1)
Primary health center	161 (30.9)
Nurse	106 (20.3)
Midwife	138 (26.4)
Self-medication	108 (20.7)
Other	3 (0.6)

Table 2: Typhoid fever according to village and demographic variables

Variable	No.of individuals	No. of patients with typhoid fever in category	Typhoid (%)	Chi-square (χ^2) p-value
Total	1957	134	6.8	-
Village				
Bonto Lebang	622	43	6.9	-
Rannaya	705	47	6.7	-
Ta'Bassi	365	26	7.1	-
Panrang-Panrang	117	8	6.8	-
Ta'Lambua	148	10	6.8	0.99
Sex				
Male	959	60	6.3	-
Female	998	74	7.4	0.35
Age				
0-4	241	0	0.0	-
5-9	170	3	1.8	-
10-14	217	21	9.7	-
15-29	641	34	5.3	-
30-44	350	36	10.3	-
45-59	185	14	7.6	-
≥60	153	26	17.0	<0.001
Education[a]				
No formal education	430	54	12.6	-
Primary school	686	47	6.9	-
Secondary school and higher	59	0	0.0	<0.001
Marital status[a]				
Unmarried	293	16	5.5	-
Married	882	85	9.6	0.04

[a]Population age ≥18 years

care center (30.9%) in Jeneponto or consulted the local nurse (20.3%) or midwife (26.4%). Self diagnosis (20.7%) and medication practiced using traditional medicines based on herbal extracts and bean-based ointments also is common. The diagnosis of typhoid had been made by one of the health workers in 122 (90%) patients. Lack of money and knowledge and absence of medical staff were major obstacles in obtaining medical care.

More women (n = 74), than men (n = 60) had attracted the illness but this difference was not statistically significant (p = 0.35). The median age of the typhoid patients was 30 years compared with 20 years for individuals that did not have the disease (p<0.001). This difference was caused by the fact that typhoid cases were not reported among infants <5 years of age and only three cases (1.8%) were reported in the age group of 5-9 years. The highest number (17%) was observed among the elderly (>60 years), but when controlling for confounding by education this association was not significant anymore. Also, marital status was not associated with the occurrence of typhoid after controlling for confounding. Limited education was highly associated with the occurrence of typhoid (p<0.001); 12.6% of those with no formal education had been ill with typhoid compared with 6.9% for those with primary school only and no cases occurred among those who had attended secondary school. Prevalence rates of other commonly occurring diseases were equal for the five villages and the occurrence of typhoid in households did not relate to the occurrence of these other diseases.

Factors that were not associated in univariate analysis with an increased risk for having typhoid were income (p = 0.9), distance to the water source used for collecting drinking water (p = 0.27), types of water source p = 0.66), type of latrine (p = 0.76) and bathing place (p = 0.36), number of persons per household (p = 0.15), eating at home (p = 0.49) and the consumption of fruit (p = 0.8). Risk factors for having typhoid fever that were identified in univariate analysis but that were not significantly any more in multivariate analysis are living in house that is of poor quality (p = 0.005), low quality of water used for bathing and brushing teeth (p<0.001), drinking water that has not been boiled (p<0.001), not washing hands before preparing food (p<0.001).

Risk factors identified in the univariate analysis that remained associated with an increased risk of having typhoid fever in multivariate logistic regression are: consumption of uncooked vegetables, consumption of water that is of poor quality, faecal contamination of water and not washing hands and not using soap when washing hands before eating (Table 3). Bathing in water with a poor quality and using water with a poor quality for

Table 3: Multivariate analysis: household and behavioural factors related with typhoid fever

Variable as risk factor	No. of households in category	Households with typhoid fever in category	aOR (95% CI, p-value)
Quality of drinking water[a]			
Good	69	16	-
Moderate	187	14	1
Bad	109	66	5.29 (2.82-991, <0.001)
***E. coli* contamination of drinking water**[b]			
No	70	11	1
Yes	295	34	4.11 (1.52-11.1, = 0.001)
Consumption of uncooked vegetables			
Always	77	70	5.31 (2.60-10.8, <0.001)
Sometimes	96	18	1
Never	192	20	
Washing hands before eating			
Yes, with soap	165	8	1
Yes, without soap	76	22	2.84 (1.18-6.86, <0.001)
Never	124	64	9.73 (4.60-20.6, <0.001)

[a]Rated by odour, colour and taste and [b]: >1 CFU/2 mL

brushing teeth, drinking of unboiled water and not washing hands before preparing food were not significant any more due to controlling of *E. coli* contaminated water as confounding factor. To determine the effect of using soap when hand washing before eating these variables were combined and stratified in not washing and washing with and without soap. The quality of the drinking water was rated bad in 29.9% of the households, 76.1% of the households had drinking water available that was bacteriological contaminated in 21.1% of the households vegetables always were eaten uncooked in 34% of the households hands were never washed before eating and finally, soap was not used for washing hands in 31.5% of the households.

Population Attributable Risk percentage (PAR%) was estimated using Levin's formula

$$P\times(OR - 1)/P\times(OR - 1) + 1$$

whereby, P is proportion in households with the risk factor (Gordis, 2000). With more risk factors per household the risk for typhoid becomes greater (Chi-square (χ^2) for trend, $p<0.001$); while no typhoid cases occurred in 47 households that did not have any of the four risk factors, one or more cases occurred in 77% of the 92 households with three or four concurrent risk factors (Fig. 1). The proportion of disease in this population that can be attributed to the risk factors was high. Population attributable risks for drinking water that is of poor quality, drinking water that is contaminated, eating uncooked vegetables, not wash hands before eating and not using soap when washing hands were 57, 51, 47, 77 and 29%, respectively. Practicing hand washing before eating showed the highest possible preventive impact.

Prevention by boiling of water had little effect on the bacteriological quality: coliform contamination (>1 Colony Forming Unit (CFU)/2 mL) was found in 75.3% of the boiled water samples compared with 80.8% of unboiled water samples collected by the same households at their preferred water source. Only about half (46.8%) of the households boils their drinking water.

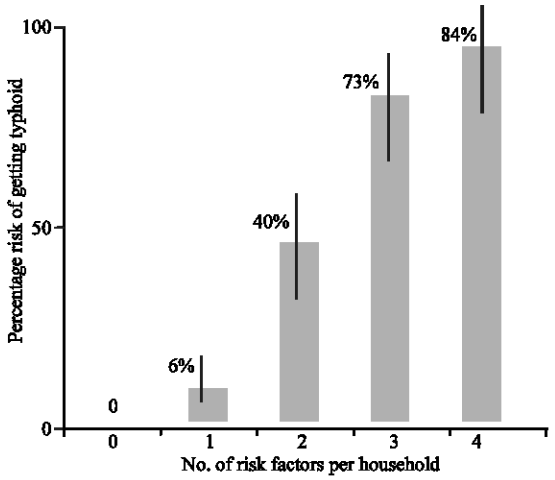

Fig. 1: Risk of developing typhoid fever for members of households with one or more risk factors

DISCUSSION

This study confirmed the very high incidence of typhoid among the rural population in South-Sulawesi. In this population, the study identified the following risk factors for typhoid: not washing hands before eating and not using soap when washing hands, consumption of raw vegetables, consumption of water that is of poor quality and consumption of water that is faecal contaminated. An earlier study performed in Semarang, the capital of Central Java, Indonesia showed that living in a house without water supply from the municipal network and with an open sewer, not washing hands before eating as well as being unemployed or having a part time job only are risk factors for getting typhoid (Gasem *et al*., 2001). In that study the quality of the water used for consumption was

not independently associated with an increased risk for typhoid. Their study however cannot be directly compared with the study was performed in a rural area lacking infrastructure for drinking water supplies and sewage containment.

Sanitation and water quality play a central role in the transmission of typhoid (Ram *et al*., 2007; Srikantiah *et al*., 2007). Raw surface water is the main source of water for drinking and bathing in most of rural South-Sulawesi and no attempts are made to clean wastewater or to prevent sewage from contamination of water sources used for consumption. The absence of sufficient toilets with drainage into closed sewer systems and the habit to use gardens, ponds and rivers for disposal of human waste add to the contamination of the environment and water sources with human excretions and hence, human pathogens. The quality of the drinking water rated by odour, colour and taste was judged acceptable in only 19% of the households. Bacteriological examination of water samples collected from drinking water containers from all households demonstrated the presence of coliform bacteria in drinking water supplies of 76.1%. Observation of boiling practice at households showed that water was not brought to a full boil and generally heated for a short period only and analysis of water samples collected before and after boiling showed a minimal effect on the bacteriological quality. Lack of knowledge and importantly lack of fuel may hamper proper boiling. The poor result of home drinking water purification was reported in a study performed in Karachi (Luby *et al*., 2000).

The risk of consumption of sewage contaminated raw vegetables was identified earlier in the studies performed in Chile and Turkey (Morris *et al*., 1984; Black *et al*., 1985; Hosoglu *et al*., 2006). The absence of proper sanitation in rural South-Sulawesi together with the practice to deposit human excretions in fields and gardens likely leads to the contamination of vegetables and the risk for disease when eating these uncooked. Several kinds of vegetables are grown that grow close to the soil.

Washing of hands with soap and clean water removes *Salmonellae* from hands (Pether and Scott, 1982). Washing hands before eating (but not washing hands before preparing food) clearly was effective in reducing the risk of disease. Soap is used for washing hands in only some households and contributes to a reduction in the risk of disease. It may be noted that washing hands was effective even though the water that is used often is contaminated.

Two other factors need attention. First, education and in particular education received at secondary school or higher also was demonstrated to be associated with less typhoid cases. Education was not included in the multivariate analysis as it is not possible to value the different levels of education of different members of one household and how this knowledge disseminates to other household members. Second, contact with (ex) patient (s) as a possible risk factor was not studied. Risk of infection was significantly higher for those who had received no formal education or had attended primary school only. At secondary school and to a lesser extend at primary school specific attention is given to personal hygiene and health. Causes of diseases and disease prevention are taught at secondary school. Illiteracy in the Jeneponto sub district is high. About one third of the teenagers and adults had no formal education and only 5% of the adults had attended secondary school or higher.

Our study indicates that knowledge obtained at secondary school helps to prevent communicable diseases such as typhoid. Education may help by improving general hygiene and avoiding risky behaviour such as not washing hands before eating, not cooking of vegetables and not selecting good quality water for drinking. Possibly a person with a better knowledge of disease transmission also avoids contact with patients or takes precautions to prevent infection. A recent contact with a (ex) patient recently was identified as an important risk factor in the study performed in the Mekong Delta, Vietnam (Luxemburger *et al*., 2002). Contacts with a (ex) patient in the Jeneponto sub-district might be frequent as almost one third of the household had a typhoid patient and several had 2 or 3 patients in 1 year. A study performed in Chile concluded that secondary cases in households are rare (Ferreccio *et al*., 1984) but this might depend on several factors including living conditions, hygiene, sanitation and knowledge to take the proper preventive measures.

Present results seemingly contrast with the finding by Velema *et al*. (1997) performed in Ujung Pandang that high-risk groups in an urban area includes those who had an university education and the notion that the incidence of typhoid peaks in schoolchildren (Bodhidatta *et al*., 1987; Yang *et al*., 2001). However, patients enrolled in the study by Velema *et al*. (1977) were enrolled in a private hospital that only can be afforded by better-off persons. Furthermore, university students may depend for their nutritional needs on food stalls where food and drinks are prepared and served under questionable hygienic conditions and schoolchildren may supplement their luncheons with drinks, ice cream and snacks offered by street vendors. Schoolchildren in the villages of the Jeneponto district eat at home and street vendors are an unknown phenomenon.

Other studies have also pointed to other risk factors and these include eating and drinking outside home and the consumption of ice cubes (Velema *et al*., 1997; Black *et al*., 1985; Luby *et al*., 1998; Castillo *et al*., 1995). However, such factors are not relevant in the villages of the Jeneponto sub-district where these eating places and such commodities are not available.

Typhoid in this study was not reported among children under five. The age depended attack rate of typhoid is controversial. In a study performed in Chile typhoid was very rare among very young children (Ferreccio *et al*., 1984). Lin *et al*. (2000) in a population based study performed in the Mekong Delta in Vietnam reported a highest attack rate in children age 5-9 years and lowest for >30 year-old. The attack rate for the children age 5-9 was about twice as high as for children age 2-4 and no cases were found among younger children. In contrast a study performed in Delhi, India showed that the attack rate in children under 5 years of age was about 2.5 times higher than in individuals age 5-19 years (Sinha *et al*., 1999). One possible explanation is that the disease in children presents as a non-specific illness and because of this was not recognized in this study and also not in the Vietnam study.

The prevalence of typhoid in South-Sulawesi is one of the highest in the world and the situation in the Jeneponto sub-district is not an exception. It might be clear that contamination of surface water, scarcity of water, absence of an adequate infrastructure for water and sewage management, poor hygienic practice and eating habits and lack of knowledge together with an abundance of carriers and patients, poverty and absence of any control programme all are debit to this situation. It should be noted that we investigated typhoid based on disease reported by household heads. In 90% the patient had consulted one of the health workers who had diagnosed the disease based on the clinical findings.

This findings thus apply to the clinical syndrome, which is consistent with typhoid fever. The villagers are well aware of the risk of developing severe disease and the need for early treatment and most will consult one of the health workers in case of persisting febrile illness. The current practice of diagnosis based on clinical signs and symptoms may have led to some degree of misdiagnosis in particular in patients with mild disease and presenting with non-specific symptoms. Misdiagnosis may have been high among those who did not consult one of the health workers. The strong associations observed (aORs ranging from 4.11-9.73) however, indicate that the risk factors identified remain valid even when part of the patients was misdiagnosed. In spite of this limitation of the study it will be clear that typhoid is an important health problem in South-Sulawesi even though the disease still can be treated well using chloramphenicol and only in rare cases complications develop.

The control of typhoid likely requires rigorous measures, which should include vaccination, improved sanitation and hygiene, the supply of clean drinking water and the elimination of carriers. However each of these measures is expensive and cannot be supported financially by the local population and will require investment by the national government or non-governmental organizations. These results suggest that education and the introduction of simple measures such as hand washing before eating, using soap when washing hands and cooking of vegetables could present an attractive and affordable alternative to control typhoid. This could be done through community health workers or by giving extra attention to this subject at schools. In spite of this, availability of clean and sufficient drinking water should be a priority but could be more difficult to achieve. Sanitation and municipal water supply systems have successfully contributed to the control of typhoid in countries were the illness once was endemic (Schoenen, 2002). Infrastructure projects to improve sanitation and to provide safe water are expensive and are unlikely to take place in the study area shortly. Vaccination also should be given priority. Vaccination for typhoid can be highly effective not only in travelers but also to control outbreaks and to control disease in endemic situations (Engels and Lau, 2000; Tarr *et al*., 1999). Vaccination for typhoid deserves consideration to control the disease in rural and urban Indonesia.

CONCLUSION

Typhoid fever remains a very important public health problem in rural areas in Indonesia. Poor sanitation and hygiene together with the absence of clean drinking water contribute to the high prevalence of this food and water born disease. Health education and information promoting the consumption of cooked vegetables, the boiling of water before consumption, the regular washing of hands before eating the use of soap, when washing hands may contribute to the prevention of typhoid fever. The building and use of pit toilets and construction of a water supply system should be prioritized. Provision of laboratory support for the local health care workers working in these remote areas in Indonesia will help to improve the diagnosis and treatment of patients and contribute to the health of the population.

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REFERENCES

Bhan, M.K., R. Bahl, S. Sazawal, A. Sinha and R. Kumar *et al*., 2002. Association between *Helicobacter pylori* infection and increased risk of typhoid fever. J. Infect. Dis., 86: 1857-1860. PMID: 12447776. http://www.journals.uchicago.edu/doi/abs/10.1086/345762.

Birkhead, G.S., D.L. Morse, W.C. Levine, J.K. Fudala and S.F. Kondracki *et al*., 1993. Typhoid fever at a resort hotel in New York: A large outbreak with an unusual vehicle. J. Infect. Dis., 167: 1228-1232. PMID: 8486960.

Black, R.E., L. Cisneros, M.M. Levine, A. Banfi and H. Lobos *et al*., 1985. Case-control study to identify risk factors for paediatric endemic typhoid fever in Santiago, Chile. Bull. World Health Organ., 63: 899-904. PMID: 3879201. http://whqlibdoc.who.int/bulletin/1985/Vol63-No5.

Bodhidatta, L., D.N. Taylor, U. Thisyakorn and P. Echeverria, 1987. Control of typhoid fever in Bangkok, Thailand, by annual immunization of schoolchildren with parenteral typhoid vaccine. Rev. Infect. Dis., 9: 841-845. PMID: 3438648. http://www.jstor.org/stable/4454175.

Castillo, M.T.G., J.T. Superable and R.L. Magpantay, 1995. Case-control study of resistant *Salmonella typhi* in Metro Manilla, Philippines. Southeast Asian J. Trop. Med. Publ. Health., 26: 39-41.

Dunstan, S.J., V.A. Ho, C.M. Duc, M.N. Lanh and C.X. Phuong *et al*., 2001. Typhoid fever and genetic polymorphism at the natural resistance associated macrophage protein 1. J. Infect. Dis., 183: 1156-1160. PMID: 11237848. http://www.journals.uchicago.edu/doi/abs/10.1086/319289.

Dunstan, S.J., H.A. Stephens, J.M. Blackwell, C.M. Duc and M.N. Lanh *et al*., 2001. Genes of the class II and class III major histocompatibility complex are associated with typhoid fever in Vietnam. J. Infect. Dis., 183: 261-268. PMID: 11120931. http://www.journals.uchicago.edu/doi/abs/10.1086/317940.

Dunstan, S.J., T.H. Nguyen, K. Rockett, J. Forton and A.P. Morris *et al*., 2007. A TNF region haplotype offers protection from typhoid fever in Vietnamese patients. Hum. Genet., 122: 51-61. PMID: 17503085. http://www.springerlink.com/content/5479ml6761795604.

Engels, E.A. and J. Lau, 2000. Vaccines for preventing typhoid fever. Cochrane Database Syst. Rev., 2: CD001261. PMID: 10796623. http://mrw.interscience.wiley.com/cochrane/clsysrev/articles/CD001261/frame.html.

Ferreccio, C., M.M. Levine, A. Manterola, G. Rodriguez and I. Rivara *et al*., 1984. Benign bacteremia caused by *Salmonella typhi* and paratyphi in children younger than 2 years. J. Pediatr., 104: 899-901. PMID:6427437.DOI:10.1061/s0022-3476(84)80492-8.

Gasem, M.H., W.M. Dolmans, M.M. Keuter and R.R. Djokomoeljanto, 2001. Poor food hygiene and housing as risk factors for typhoid fever in Semarang, Indonesia. Trop. Med. Int. Health, 6: 484-790. PMID: 11422963. http://www3.interscience.wiley.com/cgi-bin/fulltext/118999401.

Gordis, L., 2000. Epidemiology. 2nd Edn. In: Saunders, W.B. and W.R. Schmitt, New York, pp: 174-177.

Gruner, E., M. Flepp, H. Gabathuler, K.L. Thong and M. Altweg, 1997. Outbreak of typhoid fever in a non-endemic area: Comparison of 3 molecular typing methods. J. Microbiol. Methods, 28: 179-185. DOI: 10.1016.s0167.7012(97)00977-9.

Hosoglu, S., M. Loeb, M.F. Geyik, H. Ucmak and P. Jayaratne, 2003. Molecular epidemiology of invasive *Salmonella typhi* in Southeast Turkey. Clin. Microbiol. Infect., 9: 727-730. PMID: 12925118 http://www3.interscience.wiley.com/cgi-bin/fulltext/118849929.

Lin, F.Y., A.H. Vo, V.B. Phan, T.T. Nguyen and B. Bryla, 2000. The epidemiology of typhoid fever in the Dong Thap Province, Mekong Delta region of Vietnam. Am. J. Trop. Med. Hyg., 62: 644-648. PMID: 11289678. http://www.ajtmh.org/cgi/reprint/62/5/644.

Luby, S.P., M.K. Faizan, S.P. Fisher-Hoch, A. Syed and E.D. Mintz *et al*., 1998. Risk factors for typhoid fever in an endemic setting, Karachi, Pakistan. Epidemiol. Infect., 120: 129-138. PMID: 9593481. www.jstar.org/stable/3864200.

Luby, S.P., A.H. Syed, N. Atiullah, M.K. Faizan and S. Fisher-Hoch, 2000. Limited effectiveness of home drinking water purification efforts in Karachi, Pakistan. Int. J. Infect. Dis., 4: 3-7. PMID: 10689207. DOI: 10.1016/s1201-9712(00)90058-4.

Luxemburger, C., M.C. Chau, N.L. Mai, J. Wain and T.H. Tran *et al*., 2001. Risk factors for typhoid fever in the Mekong delta, Southern Vietnam: A case control study. Trans. Roy. Soc. Trop. Med. Hyg., 95: 19-23. PMID: 11280056. DOI: 10.1016/s00035-9203(01)90318-9.

Mermin, J.H., R. Villar, J. Carpenter, L. Roberts and A. Samaridden *et al*., 1999. A massive epidemic of multidrug-resistant typhoid fever in Tajikistan associated with consumption of municipal water. J. Infect. Dis., 179: 1416-1422. PMID: 10228063 http://www.journals.uchicago.edu/doi/abs/10.1086/314766.

Morris, J.G., C. Ferreccio, J. Garcia, H. Lobos and R.E. Black *et al*., 1884. Typhoid fever in Santiago, Chile: A study of household contacts of pediatric patients. Am. J. Trop. Med. Hyg., 33: 1198-1202. PMID: 6507731. http://www.ajtmh.org/cgi/reprint/33/6/1198.

Pang, T., M.M. Levine, B. Ivanoff, J. Wain and B.B. Finlay, 1998. Typhoid fever-important issues still remain. Trends Microbiol., 6: 131-133. PMID: 9587187. DOI: 10.1016/S0966-842X(98)01236-0.

Parry, C.M., T.T. Hien, G. Dougan, N.J. White and J.J. Farrar, 2002. Typhoid fever. N. Engl. J. Med., 347: 1770-1782. PMID: 12456854. http://content.nejm.org/cgi/content/extract/347/22/1770.

Pether, J.V.S. and R.J.D. Scott, 1982. Salmonella carriers: Are they dangerous? A study to identify finger contamination with *Salmonellae* by convalescence carriers. J. Infection, 5: 81-88. DOI: 10.1016/s0163-4453(82)93365-5.

Ram, P.K., A. Naheed, W.A. Brooks, M.A. Hossain and E.D. Mintz, 2007. Risk factors for typhoid fever in a Slum in Dhaka, Bangladesh. Epidemiol. Infect., 135: 458-465. PMID: 16893490. http://journals.cambridge.org/action/displayAbstract?fromPage=online&aid=939240.

Schoenen, D., 2002. Role of disinfection in suppressing the spread of pathogens with drinking water: Possibilities and limitations. Water Res., 36: 874-888. PMID:12369533.DOI:10.1016/S0043-1354(02)00076-3.

Sinha, A., S. Sazawal, R. Kumar, S. Sood and V.P. Reddaiah *et al*., 1999. Typhoid fever in children aged <5 years. Lancet, 354: 734-737. PMID: 10475185. http://www.thelancet.com/journals/lancet/article/PIIS0140-6736(98)09001-1/fulltext.

Srikantiah, P., S. Vafokulov, S.P. Luby, T. Ishmail and K. Earhart *et al*., 2007. Epidemiology and risk factors for endemic typhoid fever in Uzbekistan. Trop. Med. Int. Health, 12: 838-847. PMID: 17596250 http://www3.interscience.wiley.com/cgi-bin/fulltext/118507008.

Tarr, P.E., L. Kuppens, T.C. Jones, B. Ivanoff and P.G. Aparin *et al*., 1999. Considerations regarding mass vaccination against typhoid fever as an adjunct to sanitation and public health measures: Potential use in an epidemic in Tajikistan. Am. J. Trop. Med. Hyg., 61: 163-170. PMID: 10432074. http://www.ajtmh.org/cgi/reprint/61/1/163.

Tran, H.H., G. Bjune, B.M. Nguyen, J.A. Rottingen and R.F. Grais *et al*., 2005. Risk factors associated with typhoid fever in Son La province, Northern Vietnam. Trans. R. Soc. Trop. Med. Hyg., 99: 819-826. PMID: 16099488. http://tropicalmedandhygienejrnl.net/retrieve/pii/S0035920305001343.

Vollaard, A.M., S. Ali, S. Widjaja, H.A. Asten and L.G. Visser *et al*., 2005. Identification of typhoid fever and paratyphoid fever cases at presentation in outpatient clinics in Jakarta, Indonesia. Trans. R. Soc. Trop. Med. Hyg., 99: 440-450. PMID: 15837356. http://tropicalmedandhygienejrnl.net/retrieve/pii/S0035920305000039.

Velema, J.P., G. van Wijnen, P. Bult, T. van Naerssen and S. Jota, 1997. Typhoid fever in Ujung Pandang, Indonesia-high-risk groups and high-risk behaviours. Trop. Med. Int. Health, 2: 1088-1094. PMID: 9391512. DOI: 10.1046/j.1365-3156.1997.do1-179.

Yang, H.H., P.E. Kilgore, L.H. Yang, J.K. Park and Y.F. Pan *et al*., 2001. An outbreak of typhoid fever, Xing-an County, People's Republic of China, 1999: Estimation of the field effectiveness of Vi polysaccharide typhoid vaccine. J. Infect. Dis., 183: 1775-1780. PMID: 11372030. http://www.journals.uchicago.edu/doi/abs/10.1086/320729.