# Association of clinical features of typhoid fever with socioeconomic status in Pakistan

Muhammad Samsoor Zarak,<sup>1</sup> Hamaiyal Sana,<sup>2</sup> Muzhgan Shah,<sup>2</sup> Shabir Lehri,<sup>2</sup> Mahekan Saghir,<sup>2</sup> Qandeel Gul,<sup>2</sup> Muhammad Saood,<sup>3</sup> Aqeel Nasim<sup>3</sup> and Noman ul haq<sup>3</sup>.

<sup>1</sup>West Virginia University Health Sciences Centre, Morgantown, West Virginia, United States of America (Correspondence to: M Samsoor Zarak: samzarak@gmail.com). <sup>2</sup>Bolan Medical College, Brewery Road, Quetta, Pakistan. <sup>3</sup>Department of Pharmacy Practice, University of Balochistan, Quetta, Pakistan.

## Abstract

**Background:** Typhoid fever is spread by ingestion of contaminated food or water, which is linked to infrastructure; specifically, sewage and sanitation. In developing countries, infrastructure varies according to socioeconomic status (SES). Balochistan is the least developed province of Pakistan.

Aims: To analyse the association between the clinical features of typhoid fever and socioeconomic status.

**Methods:** A quantitative, cross-sectional study was conducted in Quetta, Balochistan, Pakistan. Between May and October 2017, 143 patients presented to tertiary care hospitals and private clinics with a complaint of fever lasting ~3 days, along with a clinical history of headache, malaise, diarrhoea or constipation, abdominal pain, dry cough, and anorexia. All patients had a positive blood culture for *Salmonella enterica* serotype Typhi. Eighteen patients dropped out of the study, leaving 125.

**Results:** Seventy (56%) participants had low socioeconomic status (SES), 40 (32%) middle SES and 15( 12%) high SES. The strongest predictors of presenting with typhoid fever were patients' clinical condition when presenting to health facilities, followed by SES. Most respondents had a treatment duration of 1–2 weeks. SES had a high impact on source of drinking water supply.

**Conclusion:** The strongest predictor of reporting typhoid fever was the current clinical condition of the patients, followed closely by SES. The incidence of typhoid fever in the low SES patients was almost the same as in the middle and high SES patients. Patients with low SES were more susceptible to contracting typhoid fever due to poor health status and facilities. Keywords: Balochistan, socioeconomic status, typhoid fever, enteric fever, Pakistan.

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## Introduction

Typhoid fever is a severe illness caused primarily by Gram-negative Salmonella enterica serotype Typhi (1). It is indicated by nonspecific symptoms such as continuous fever, headache, nausea, poor appetite, lethargy, diarrhoea and sometimes constipation (2). Other clinical features include splenomegaly, hepatomegaly, rose spots, and lethal intestinal perforation (1). It is contracted via the faecal-oral route by ingestion of food or water contaminated with Salmonella species. Poor hygiene and sewage are considered to be contributing factors. The global burden of typhoid fever over the past few decades shows that there are 21.6 million cases globally and ~216 500 deaths annually (3). The annual incidence of typhoid fever in Asia is > 100/100 000 cases (4). More than 90% of typhoid fever cases arise from South and Southeast Asia (3), mainly Pakistan, India, China, Indonesia and Viet Nam, where the disease is still considered to be endemic (4).

Pakistan is a developing country with a rapidly growing population and less than satisfactory water, food and hygiene measures that result in a flourishing habitat for infectious diseases. According to a study in 2013 in Quetta, 18.6% of paediatric patients had positive serological tests for typhoid fever (5). In Karachi, the incidence of typhoid fever was 710/100 000 when diagnosed by serological tests, and almost 170/100 000 when diagnosed by blood culture (6).

Health issues are frequently related to socioeconomic status (SES), which serves as a reliable indicator of population mortality and morbidity (7). Most studies have shed light on health-related issues associated with low SES; mainly because individuals with low SES are more susceptible to illness and death compared with middle and high SES. Typhoid fever remains a poorly characterized disease, with uncertain and often inaccessible methods of diagnosis and lack of data about the total global burden (8). It is hard to understand the incidence and prevalence patterns of typhoid fever among the population due to its often random occurrence without much distinction for SES or age.

The present study is believed to be the first to analyse the association of typhoid fever and its clinical features, such as signs and symptoms, duration and treatment, with SES.

## Methods

#### Study design and population

This was a questionnaire-based quantitative, cross-sectional study conducted in Quetta, Balochistan, Pakistan. Between May and October 2017, 143 patients presented to tertiary care hospitals and private clinics with a complaint of fever lasting  $\sim$ 3 days, along with a clinical history of headache, malaise, diarrhoea or constipation, abdominal pain, dry cough, and anorexia. All patients had a positive blood culture for *S*. Typhi. Participants were interviewed and their answers were recorded. Eighteen patients dropped out of the study, leaving a total of 125.

#### **Ethical considerations**

Informed consent was obtained from the patients for publication of this study at the time of interview. The study was reviewed by the Institutional Review Board of Bolan Medical College, Quetta.

#### Study tool

The study tool was a self-designed pro forma divided into 3 sections: (1) informed consent; (2) demographic characteristics of patients; and (3) questionnaire comprising 23 questions (6 on SES, 4 on personal hygiene and 13 on clinical aspects of typhoid fever). The first 9 questions had several options and only 1 was to be circled as an answer, whereas the last 14 required written statements.

#### Data analysis

The statistical analysis was done using SPSS version 20. Statistical significance was determined by  $\chi^2$  test and *P* value (< 0.05). A regression model was used to establish the association of clinical features of typhoid fever with SES.

## **Results**

#### **Demographic characteristics**

Ninety-one patients (72.8%) were aged 1–30 years and 73 (58.4%) were female (Table 1). Forty-six (36.8%) patients were illiterate and 34 (27.2%) were employed by the government on low wages. Fifty-six (44.8%) patients belonged to nuclear families; 75 (60%) owned their houses and 56 (44.8%) had newly constructed cement rather than traditional mud houses.

#### Water supply

Most of the participants (n = 92; 73.6%) used tap water for drinking and 33 (26.4%) used filtered water.

#### **SES**

SES was based on a 2006 definition (9): low SES was an income of 4000–20 000 Pakistani rupees (PKR); middle SES was 50 000–100 000 PKR; and high SES was > 100 000 PKR. There were 70 (56%) participants with low SES, 40 (32%) with middle SES and 15 (12%) with high SES.

Table 1 Demographic characteris	tics		
Demographic characteristics	No. of patients	Percentage	
Age (years)			
1-30	91	72.8	
31-60	30	24	
61-90	4	3.2	
Sex			
Male	52	41.6	
Female	73	58.4	
Education			
None	46	36.8	
High school or under	51	40.8	
Undergraduate	17	13.6	
Postgraduate	11	8.8	
Occupation			
Government	34	27.2	
Student	33	26.4	
Labourer	18	14.4	
Business/landlord	5	4.0	
Housewife	23	18.4	
Not mentioned	12	9.6	
Type of family			
Nuclear	56	44.8	
Extended	42	33.6	
Not mentioned	27	21.6	
House occupancy			
Owned	75	60.0	
Rented	43	34.4	
Not mentioned	7	5.6	
House construction			
Mud	54	43.2	
Cement	56	44.8	
Not mentioned	15	12.0	

#### **Clinical features**

Most of the participants (n = 93; 74.4%) had a first-time infection (Table 2). Ninety-four (75.2%) reported improvement in their health after initiating treatment, and 91 (72.8%) reported that duration of illness was < 1 month. Forty-three (34.4%) participants were prescribed a combination of antibiotics and analgesics, and 77 (61.6%) used only cephalosporin. The duration of treatment for 101 (80.8%) patients was 1–2 weeks.

#### Signs and symptoms

Most of the patients presented with fever (n = 123; 98.4%), 112 (89.6%) with nausea or vomiting, and 114 (91.2%) with diarrhoea (Table 3).

#### **Typhoid fever and SES**

Most respondents had treatment duration of 1–2 weeks, which was significantly more likely in patients with low or middle SES (P = 0.006) (Table 4). Unsatisfactory personal hygiene was significantly associated with low and middle SES (P = 0.000). Eating outside was significantly more common in patients with low or middle SES (P = 0.008). Use of complementary medicine was significantly more common in patients with low or middle SES (P = 0.006).

#### Table 2 Clinical features of patients with typhoid fever

Clinical aspects	No. of patients	Percentage
Type of infection		
First time	93	74.4
Relapse	32	25.6
Current condition		
Improved	94	75.2
Not improved	13	10.4
Uncertain	18	14.4
Duration of disease		
< 1 month	91	72.8
1–3 months	27	21.6
4–6 months	1	0.8
1-2 years	1	0.8
> 2 years	1	0.8
Uncertain	4	3.2
Drugs		
Antibiotic	13	10.4
Antibiotic + analgesic	43	34.4
Antibiotic +analgesic + antinausea	19	15.2
Antibiotic + analgesic + antacid	35	28.0
Antibiotic + analgesic + antinausea +	7	5.6
antacid	4	3.2
Antibiotic + antinausea	4	3.2
Antibiotic + analgesic + antidiarrhoeal		
Antibiotics		
Cephalosporin	77	61.6
Quinolone	19	15.2
Penicillin	2	1.6
Other types	4	3.2
Cephalosporin + quinolone	7	5.6
Cephalosporin + penicillin	2	1.6
Cephalosporin + any other	10	8.0
Cephalosporin + quinolone + any other	4	3.2
Duration of treatment		
1-14 days	101	80.8
15-28 days	10	8.0
<1 month	13	10.4
Uncertain	1	0.8

Table 3 Signs and	symptoms in	patients with t	vphoid fever

Complications	No. of patients	Percentage
Fever		
Febrile	123	98.4
Nonfebrile	2	1.6
Pain		
Headache	23	18.4
Abdominal pain	37	29.6
Body ache	19	15.2
Headache, body ache	14	11.2
Headache, abdominal pain	11	8.8
Body ache, abdominal pain	18	14.4
Headache, abdominal pain, body ache	3	2.4
Nausea/vomiting		
Present	112	89.6
Absent	13	10.4
Diarrhoea/loose motion		
Present	114	91.2
Absent	11	8.8

## Demographic factors associated with water supply in patients with typhoid fever

Personal hygiene showed a significant association with the source of water supply (P = 0.000). Socioeconomic status SES also showed a significant association with source of water supply (P = 0.000).

## Regression analysis of association of SES and Clinical features of typhoid fever

The strongest predictor of reporting typhoid fever was patients' current condition, with an odds ratio (OR) of 1.3 [95% confidence interval (CI) 0.76–2.1] (Table 5). SES was the next strongest contributing factor (OR 1.2, 95% CI 0.68–2.2). This indicated that patients who had typhoid fever were more likely to report signs and symptoms than those who did not have signs and symptoms, after controlling for all other factors in the model. The OR for infections was 0.87, indicating that for every additional typhoid infection, respondents were 0.87 times less likely to report it, after controlling for other factors in the model.

#### Discussion

SES is a reliable indicator of morbidity and mortality, and serves as a predictor for society as a whole (10). Since the 19th century, a lot of work has been done to discover the relationship between social and health status. Multiple indicators are used to measure SES in a community, including occupation, education and income/wealth. To understand better the intricacies of SES, these indicators need to be considered all at once, along with others affecting the economic and living conditions of the population (11). Our study considered the dimension of income to classify SES in accordance with a detailed study conducted in 2006, defining the income groups in Pakistan (9). The dimensions of education and occupation were also included to gain a better understanding of the association.

We observed that most of the patients diagnosed with typhoid fever were aged 1–30 years, which confirmed previous findings (12), and 56% of the patients had low SES. It was also observed that 36.8% of patients were uneducated. Most of the patients were employed; however, their SES was not dictated by whether they were employed but rather by their income. Although patients with middle and high SES were diagnosed with typhoid fever, their comparatively better living conditions with regard to water and food supply, as well as their awareness of seeking timely medical attention, gave them a better chance of avoiding the disease and its consequences.

Most of the patients diagnosed with typhoid fever had unfiltered water supplies, which supports the fact that water and food sources are the most common methods of transmission (13). We also observed that people with high SES had mostly filtered water resources but nevertheless succumbed to the disease, indicating other risk factors

#### Table 4 Typhoid fever and SES

	Socioeconomic class			Р
	High	Low	Middle	
Disease duration				
>< 1 month	15	44	32	0.354
1–3 months	0	20	7	
4–6 months	0	1	0	
1-2 year	0	1	0	
> 2 years	0	1	0	
Uncertain	0	3	1	
Freatment duration				
1 day	0	0	1	0.006
2-3 days	0	16	5	
4-7 days	0	11	3	
1–2 weeks	11	31	23	
3-4 weeks	4	1	5	
1–2 month	0	10	2	
> 2 months	0	1	0	
Uncertain	0	0	1	
Personal hygiene				
Satisfactory	15	1	26	0.000
Not satisfactory	0	69	14	
Habit of eating outside				
Frequently	13	29	26	0.008
Not likely	2	20	8	
Failed to mention	0	21	6	
Cause of treatment-seeking delay				
Burden of studies	0	0	2	
Failed to mention	0	11	4	0.221
Lack of awareness	0	3	1	
Lack of facilities	0	7	1	
Misdiagnosed	0	2	0	
None	15	46	31	
Self-medication	0	0	1	
Took a break because of pregnancy	0	1	0	
Complementary medicine tried				
Yes	2	20	4	0.006
No	12	29	29	
Failed to mention	1	21	7	

like food and hygiene practices. Cephalosporin was a popular choice of treatment, and in some cases, empirical therapy was undertaken to cure symptoms.

SES also had a significant effect on duration of treatment and was shorter in patients with high compared with middle or low SES. The duration of treatment for some patients with low or middle SES lasted for several months. This confirms the explanation that people with high SES have the awareness and basic facilities to seek early medical intervention. Furthermore, some participants had a considerable period of delay before seeking medical intervention. The most common reason besides lack of facilities was lack of awareness regarding the disease and its basic signs and symptoms.

Demographic factors		Source of water supply	
	Tap water	Filtered water	<b>P</b> *
Hygienic practices			
Satisfactory	21	21	0.000
Not satisfactory	71	12	
Eating habits			
Healthy	44	24	0.019
Unhealthy	23	7	
Failed to mention	25	2	
Socioeconomic status			
High	5	10	0.000
Low	65	5	
Middle	22	18	

Patients, especially those with low SES, were in the habit of seeking treatment with complementary medicine.

SES played a significant role in patients' hygiene, indicating poor hygienic practice in those with low SES. Typhoid fever was most commonly observed in patients with low SES but it was also seen in those with high SES, which suggests that SES does not necessarily dictate the causative pattern of typhoid fever. Its occurrence in less-privileged people is understandable due to lack of education regarding the disease and collective poor living conditions and health facilities. The fact that typhoid fever affects the middle and high SES groups in roughly the same measure gives it a unique and confounding causative pattern.

The largest contributor to reporting a case of typhoid fever was the current condition of the patients, followed closely by SES. We also observed that patients who had typhoid fever were more likely to report signs and symptoms of the disease than were those who did not have signs and symptoms, after controlling for other factors in the model.

One limitation of the present study was that it was based on a small sample. Further research in a larger populationbased study may give better and more consistent results.

## Conclusion

Typhoid fever remains one of the most poorly characterized diseases even today. This is mainly due to the lack of data on the global burden of the disease and controversies regarding the accuracy of the diagnostic tests, and lack of awareness in the general population. Our study concluded that the largest contributor to reporting typhoid fever was the current condition of the patients followed closely by SES. We showed that the incidence pattern of typhoid fever had no distinction for SES and the disease affected people with low SES in almost the same measure as those with middle and high SES. However, patients with low SES are more susceptible to contracting typhoid fever with more distressing signs, symptoms and disease duration due to meagre health education and facilities. There is a need for health professionals and the general population to address typhoid fever, prioritizing low and middle SES and poor health facilities, which pose a threat as great as multidrug-resistant bacteria.

#### Funding: None.

**Competing interests:** None declared.

## Lien entre le tableau clinique de la fièvre typhoïde et le statut socio-économique au Pakistan

## Résumé

**Contexte** : La fièvre typhoïde se propage par ingestion d'eau ou d'aliments contaminés, elle-même liée aux infrastructures, et plus particulièrement aux systèmes d'égout et d'assainissement de l'eau. Dans les pays en développement, les infrastructures varient en fonction du statut socio-économique. Le Baloutchistan est la province la moins développée du Pakistan.

**Objectifs** : Analyser le lien entre le tableau clinique de la fièvre typhoïde et le statut socio-économique des patients.

**Méthodes** : Une étude transversale quantitative a été menée à Quetta, au Baloutchistan (Pakistan). Entre mai et octobre 2017, 143 patients ont consulté dans des hôpitaux de soins tertiaires et des cliniques privées pour une fièvre qui persistait depuis environ trois jours, accompagnée d'antécédents cliniques de céphalées, de malaise, de diarrhée ou de constipation, de douleurs abdominales, de toux sèche et d'anorexie. Tous les patients présentaient une hémoculture positive pour la *Salmonella enterica* sérotype *Typhi*. Dix-huit patients ont quitté l'étude, qui s'est poursuivie avec les 125 restants.

**Résultats** : Soixante-dix participants (56 %) avaient un statut socio-économique faible, 40 (32 %) avaient un statut moyen et 15 (12 %) avaient un statut élevé. L'état clinique des patients lors de leur arrivée dans les établissements de santé, suivis par le statut socio-économique étaient les principaux facteurs prédictifs de consultation pour symptômes de fièvre typhoïde. La plupart des participants ont reçu un traitement dont la durée était d'une à deux semaines. Le statut socio-économique avait un impact important sur la source d'approvisionnement en eau potable.

**Conclusion** : Le principal facteur prédictif de déclaration de symptômes de fièvre typhoïde était l'état clinique des patients au moment de leur arrivée dans l'établissement de santé, suivi de près par le statut socio-économique. L'incidence de la fièvre typhoïde chez les patients de faible statut socio-économique était presque la même que chez les patients de statut moyen ou élevé. Les patients ayant un statut socio-économique faible étaient plus susceptibles de contracter la fièvre typhoïde en raison de leur mauvais état de santé et d'installations sanitaires médiocres.

## الارتباط بين السهات السريرية لحمى التيفود والوضع الاجتماعي والاقتصادي في باكستان

محمد سمسور زراك، حمايال ثناء، مرَّكان شاه، شبير لهري، ، ماهيكان صغير، قنديل جل، محمد سعود، عقيل نسيم، نعمان الحق

#### الخلاصة

الخلفية: تنتشر حمى التيفود عن طريق تناول أغذية أو مياه ملوثة، وهو ما يرتبط بالبنية التحتية؛ وعلى وجه التحديد، مياه المجاري والصرف الصحي. وفي البلدان النامية، تتفاوت البني التحتية حسب الوضع الاجتماعي والاقتصادي. وتُعدُّ بلو شستان المقاطعة الأقل تنمية في باكستان.

**الأهداف**: هدفت هذه الدراسة الى تحليل الارتباط بين السمات السريرية لحمى التيفود والوضع الاجتهاعي والاقتصادي.

<mark>طُرق البحث</mark>: أُجريت دراسة كمية مقطعية في كويتا، ببلوشستان، باكستان. وفي الفترة ما بين مايو / أيار و أكتوبر/ تشرين الأول 2017، قَدم 143 مريضًا إلى مستشفيات الرعاية التخصصية والعيادات الخاصة بشكوى من حمى استمرت 3 أيام تقريبًا، إلى جانب وجود سوابق سريرية تمَثلت في الصداع، والتوعُّك، والإسهال أو الإمساك، وآلام البطن، والسعال الجاف، وفقدان الشهية. وكانت نتيجة مزرعة الدم التي أُجريت لجميع المرضى للكشف عن السلمونيلا المعوية من النمط المصلي التيفيّ إيجابية. وخرج ثمانية عشر مريضًا من الدراسة تاركين 2017 آخرين.

النتائج: كان الوضع الاجتهاعي والاقتصادي منخفضًا لدى سبعين مشاركًا (56٪)، بينها كان متوسطًا لدى 40 مشاركًا (32٪)، ومرتفعًا لدى 15 مشاركًا (12٪). وكانت أقوى العوامل المنبئة في التبليغ بحمى التيفود الحالة السريرية للمرضى عند قدومهم إلى المرافق الصحية، يتبعها وضعهم الاجتهاعي والاقتصادي. واستمرت مدة العلاج لدى معظم المستجيبين مدة تتراوح بين أسبوع واحد وأسبوعين. وكان للوضع الاجتهاعي والاقتصادي تأثير كبير على مصدر إمدادات مياه الشرب.

**الاستنتاجات**: كان العامل المنبئ الأقوى في التبليغ بحمى التيفود هو الحالة السريرية الحالية للمرضى، يليها مباشرة الوضع الاجتهاعي والاقتصادي. وكان معدل الإصابة بحمى التيفويد في صفوف المرضى من ذوي الوضع الاجتهاعي والاقتصادي المنخفض مماثلا تقريبًا لنظيره في صفوف المرضى من ذوي الوضع الاجتهاعي والاقتصادي المتوسط والمرتفع. وكان المرضى من ذوي الوضع الاجتهاعي والاقتصادي المنخفض أكثر عرضة للإصابة بحمى التيفود بسبب تدني الوضع الصحي والمرافق.

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