Introduction
Typhoidal Salmonella (Salmonella enterica serovars Typhi and Paratyphi A, B, C) are gram-negative bacilli that usually present as undifferentiated febrile illness. Salmonella osteoarticular infections are common in sickle cell anaemia and immunocompromised hosts. However, Salmonella osteomyelitis has also been reported in immunocompetent individuals. We present an immunocompetent patient with nalidixic acid-resistant Salmonella paratyphi A (NARST) spondylodiscitis.

Case History
A 57-year-old banker presented with high-grade fever for 6 weeks and severe backache for 4 weeks. He went on frequent official trips to different cities and had history of consuming foods in restaurants on these trips. He denied history of diarrhoea, joint pain, weight loss, bowel/bladder incontinence, urinary retention and motor weakness. He was a known case of systemic hypertension for 17 years and diabetes mellitus for 1 month and was on regular medicines.

Examination of the spine revealed lower thoracic tenderness and restricted lateral flexion. He had Class I obesity (body mass index 33). Blood investigations showed high erythrocyte sedimentation rate and mildly elevated C-reactive protein levels. In this patient with subacute history of back pain and fever, we considered differential diagnoses of infective spondylodiscitis, epidural and paraspinal abscess. Magnetic resonance imaging showed contrast enhancement in the 11th and 12th thoracic vertebra and intervening disc. Computed tomography-guided biopsy from thoracic vertebra showed necrotic bone with lymphocyte and neutrophil infiltration. Widal test was positive for Salmonella paratyphi A in 1280 dilutions.

Drug susceptibility testing showed sensitivity to chloramphenicol, ceftriaxone, trimethoprim-sulfamethoxazole and azithromycin. Minimum inhibitory concentration (MIC) for ciprofloxacin and azithromycin were 0.5 µg/dL and 8 µg/dL, respectively. We started injection azithromycin 1 g intravenously once daily. However, computed tomography-guided biopsy from thoracic vertebra showed necrotic bone with lymphocyte and neutrophil infiltration. Biopsy specimen and blood culture showed growth of NARST.

Keywords: Salmonella osteomyelitis, Salmonella paratyphi A, Salmonella spondylodiscitis

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he continued to have high-grade fever 1 week after initiation of azithromycin. Reasons for persistent fever that we thought of were metastatic and endovascular foci of infection and suboptimal antibiotic delivery due to poor bone penetration. Echocardiogram, ultrasound abdomen and bone scan were normal. In view of clinical failure with azithromycin, we decided to start intravenous ceftriaxone (2 g once daily) and oral trimethoprim-sulfamethoxazole (800/160 mg) twice daily. Defervescence occurred 5 days after initiation of ceftriaxone. He was seen by spine surgeons who advised conservative management. He was managed with intravenous azithromycin and ceftriaxone for 2 weeks followed by oral azithromycin (1 g once daily), ciprofloxacin (750 mg twice daily) and trimethoprim-sulfamethoxazole for 10 weeks. At his 3-month follow-up, back pain had decreased by 90%. Repeat MRI spine showed disease regression.

### Discussion

Gram-negative organisms account for 12% of vertebral osteomyelitis, and Enterobacter species, Acinetobacter baumannii and Pseudomonas aeruginosa are usually implicated. Salmonella accounts for 50% of acute osteomyelitis in sickle-cell patients. Bone infarcts, autosplenectomy and hypocomplementemia predispose to infections in sickle cell disease.

Though Staphylococcus aureus and Mycobacterium tuberculosis are common pathogens causing spondylodiscitis, infections due to Salmonella have also been described. Salmonella vertebral osteomyelitis may have been underdiagnosed, as imaging-guided/open surgical biopsy is required to confirm the diagnosis. In the absence of microbiological diagnosis, many patients may have been treated with empirical therapy directed against Mycobacteria or gram-positive organisms.

Amritanand et al. reported 11 patients with typhoidal Salmonella spondylodiscitis treated with 12 weeks of antibiotics. Half required surgery due to pain or osseous instability, and 91% (10/11) had good outcomes after 1 year.

Rohilla et al. reported a 17-year-old immunocompetent patient with Salmonella typhi spondylodiscitis initially treated with empirical anti-tuberculous therapy. He was eventually managed with cefuroxime and decompressive laminotomy.

In a review of 44 cases of Salmonella vertebral osteomyelitis, common vertebrae involved were lumbar (50%) and thoracic (20%). Diarrhoea and abdominal pain were present in merely 16% and 8%, respectively. Vertebral osteomyelitis led to neurological deficits in 8%. Cervical/Thoracic vertebral involvement, epidural abscess, S. aureus osteomyelitis and CRP levels >150 mg/L are associated with motor weakness in vertebral osteomyelitis.

Management of osteomyelitis poses a therapeutic challenge for clinicians. Poor vascularity of necrotic bone leads to reduced antibiotic delivery to infective focus. Our case report shows that antibiotic choice should be based upon drug sensitivity, bone penetration and synergism between antibiotics. Azithromycin is concentrated in macrophages and neutrophils, with low plasma and bone concentration. Azithromycin MIC ≤ 16 µg/mL is considered susceptible for invasive Salmonellosis. However, there is a lack of clinically validated MIC cut-off for azithromycin for Salmonella infections.

Garazinno found that bone penetration of ceftriaxone was adequate in cancellous bone but low in cortical bone. Trimethoprim-sulfamethoxazole is used as monotherapy for Staphylococcal osteoarticular infections. Trimethoprim attains 50% of plasma concentration in bone, whereas concentrations in synovial fluid and plasma are similar. Ciprofloxacin has excellent bone penetration and has been used as monotherapy and combination therapy in pyogenic osteomyelitis.
At primary care level, it is important to identify patients with infectious cause of back pain. Primary care physicians should look for fever, localized spine tenderness and restricted spine motion to identify these patients. These patients require urgent spine imaging and specialist referral to prevent complications.

Incidence of spondylodiscitis is likely to increase in parallel to the surge in number of organ transplants, intravascular devices and invasive spinal procedures. Typhoidal Salmonella can cause vertebral osteomyelitis in immunocompetent patients. Obtaining a microbiological diagnosis is an essential step in management. Treatment is challenging due to long duration of antimicrobial therapy, drug resistance, variable drug delivery to infected focus and risk of neurological complications.

Key Messages
Salmonella spondylodiscitis in immunocompetent hosts is an underdiagnosed entity. Imaging-guided biopsy/open surgical biopsy and culture are required to establish a diagnosis and obtain antibiotic susceptibility profile. Infective spondylodiscitis due to Salmonella poses a therapeutic challenge due to poor antibiotic bone penetration, resistant pathogens and risk of neurological complications.

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Conflicts of interest
There are no conflicts of interest.

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