#### Early infection of bilateral Total Knee Arthroplasty with Salmonella Typhi. 2 3 Case report and review of literature.

4

Abstract- Acute Salmonella Typhi prosthetic joint infection (PJI) is a rare event. In 5 Endemic areas one needs to be cautious if the patient is immunocompromised. We report a 6 case of bilateral simultaneous PJI of the knee in a 60-year-old lady who was not 7 immunocompromised. The patient presented on Post op Day 5 with Fever and local signs 8 suggestive of infection. As this was an Early PJI she was successfully treated with 9 Debridement, Poly exchange and Intravenous and oral antibiotics for 6 weeks. This case 10 highlights the fact that in patients living in these areas and in seasons where incidence of 11 12 enteric fever is high, patients should be screened preoperatively for Salmonella infection by history and stool cultures. To our knowledge this is the first case report of Early 13 Bilateral Simultaneous infection with Salmonella typhi. 14

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Keywords: Debridement, immunocompromised, Salmonella typhi, prosthetic joint infection 16 17 X,

#### Introduction 18

Periprosthetic Joint infection(PJI) is a devastating complication and can result in 19 Amputation. Staphylococcus Aureus is commones organism (1-2), PJI with 20 salmonella species being culprit only for 0.2-1% of cases (3-4), Salmonella 21 infection is common in immunocompromised patients (5-6). Other species of 22 salmonella-like enteritis and typhimurium have been reported in such patients 23 (7). There have been 4 prior instances of PJI (8) with salmonella typhi in the 24 English Literature but none of them had an acute presentation. We present a rare 25 case of early periprosthetic joint infection of bilateral total knee arthroplasty 26 with Salmonella typhi. To our knowledge this is the first case of Early Bilateral 27 Simultaneous infection with Salmonella typhi described so far. 28

**Case Report:** A 75 years old woman was diagnosed with severe osteoarthritis 29 30 of both knee joints. Medical history was not significant. Simultaneous bilateral total knee replacement was performed. Post-operative X-rays showed normal 31 alignment (Fig 1-3) She was mobilized on day one. Her post-operative recovery 32 was uneventful. She was discharged from the hospital on 7<sup>th</sup> post-operative day. 33

On the 12th post-operative day she complained of severe pain in both the 34 knee joints associated with high grade intermittent fever and generalised 35 weakness. Clinically she presented a reduction in the knee range of motions on 36 both sides. The symptoms progressed. She presented to us on 15<sup>th</sup> day. On 37 examination she was febrile with tachycardia and her blood pressure was 38 120/70mm of Hg. Local aspect showed redness and warmth. Active discharge 39 40 was seen in the right knee surgical wound which was purulent in nature. Her total White blood cells (WBC) count was 19,000/ cu-mm with increased 41 Neutrophil count of 79%. (Fig-)X-ray of both knee joints showed no signs of 42 loosening osteolysis. Preliminary culture from wound swab obtained from the 43 right knee grew moderate growth of Gram negative bacilli on culture which was 44 identified as Salmonella Typhi (Table 1); the isolate was sensitive to ampicillin, 45 ciprofloxacin, levofloxacin, cefotaxime, ceftriaxone, nalidixic acid and 46 cotrimoxazole. 47

Debridement, lavage and polyethylene insert exchange was done for the 48 right knee and the implants were stable. Purulent material and synovial tissue 49 were sent for microbiological examination. Purulent material was aspirated 50 form the left knee and similar procedure was done as well. Both the samples 51 grew scanty growth of Salmonella Typhi, the isolate had same antibiogramm. 52 Further diagnostic work up was done on 5<sup>th</sup> day of admission with Widal test 53 which revealed antibody titres of up to 1: 160 dilutions and 1: 5120 dilutions for 54 O and H antigen respectively which was suggestive of acute typhoid fever. No 55 pathogenic organisms were isolated on stool and urine culture. Antibiotic 56 therapy was started with intravenous ceftriaxone for 2 weeks and oral 57 ciprofloxacin for 6 weeks immediately after the culture report was obtained. 58

Postoperatively, the patient's general condition improved. The fever had 59 subsided and pain in the knees decreased. She was mobilised and knee range of 60 motion was started. Her blood parameters returned to normalcy. She had 61 delayed wound healing which required regular dressings. Intravenous 62 ceftriaxone was administered for two weeks and oral ciprofloxacin was 63 continued for six weeks. Subsequent microbiological examination with wound 64 swab cultures (on day 10<sup>th</sup> and 13<sup>th</sup> of admission) from both knees showed no 65 growth. At 6<sup>th</sup> week, serological follow up with Widal test showed reduced 66 antibody titres to O and H antigens up to 1: 40 dilutions and 1: 320 dilutions 67 68 respectively. Her symptoms had considerably reduced and the surgical wound showed healing with no active signs of discharge. Stool culture done on follow 69

up at 8<sup>th</sup> week was negative for Salmonella Typhi and antibody titres on Widal 70 test was less than 1:80 and up to 1:80 for O and H antigens respectively 71 showing decrease which was suggestive for resolution. At 2 years follow 72 up, patient was asymptomatic and her range of motion was 0-95 degrees in both 73 knees. There were no recurrences of *Salmonella Typhi* infection(fig 4 and 5). 74 She presented at 2 and half years with pain and swelling of left knee, Aspirate 75 76 of knee did not grow any organism -extensive work up did not reveal cause of infection and was treated with two stage procedure and underwent distal 77 Femoral replacement. After 1 year of distal femoral replacement, she was 78 79 asymptomatic (fig 6 and 7)

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#### 81 **Discussion:**

Salmonella infection of TKR is a very rare event, accounting for 0.2% of 82 periprosthetic joint infections. A PubMed search reveals 44 published cases of 83 salmonella species infections out of which 32 were in the hip and 12 were in the 84 knee. The majority (43/44) was caused by non- typhoid Salmonella (NTS) and 85 only one was caused by S. Typhi (8). The higher incidence seen with NTS is 86 because these bacteria have a wider distribution and can manifest with 87 bacteraemia and extra intestinal manifestations (9,10). The usual presentation in 88 patients without knee replacement is reactive arthritis after enteric fever and in 89 90 very rare cases septic arthritis (11, 12). All the infections by Salmonella reported so far presented between 4 months to 9 years after surgery 9(8,13,14) 91 but none had an early presentation with S typhi. In previously reported cases 92 with Salmonella 50 % had an underlying immunosuppressive condition (7,15)-93 S. typhi is mainly acquired through orofecal contamination with Gastrointestinal 94 tract being primary focus via hematogenous spread it can go to the joints 95 (16,17). There was no reported case following direct inoculation (18). Our 96 patient did not have preoperative symptoms to suggest S. typhi, it is difficult to 97 say if she was carrying the bacteria, as that work up is not routinely done for 98 joint arthroplasty. Also, patient did not have sickle cell trait or any other 99 immunocompromised state (19). The only other case of Bilateral Simultaneous 100 infection with S. typhi was described on a..... years old patient whom 101 presented delayed infection at 10 months after surgery. And she was treated by 102 Immunomodulators (8) because of a ..... disease (17,20,21). In absence of 103 104 defined protocols infection was treated with 6 weeks of antibiotics (17,20,21). Incidence of typhoid burden in India was 377 per 100,000-person years of 105

typhoid (22). Pachore et al (23)have reported that infection is the second
commonest cause of revision knee surgery and with India being in endemic
zone, its more likely to encounter cases of PJI caused by S. typhi..

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110 Conclusion-

111 This is a rare event and can cause considerable morbidity. Based on our experience we propose that in areas where Salmonella is endemic/seasonal, one 112 should ask a detailed history to see if patient had contact with typhoid patient 113 and carry out stool cultures. If stool cultures pick up a salmonella carrier then 114 patient should be treated accordingly. This might add cost at upfront but it is 115 better to treat infection prior to surgery and avoid PJI. To the best of our 116 knowledge this is the only case report in English Literature of Early Bilateral 117 Simultaneous infection with Salmonella typhi. 118

#### 119 **Consent Disclaimer:**

120 As per international standard or university standard, patient's consent has been

121 collected and preserved by the authors.

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- 125 **Conflicts of interest**
- 126 There are no conflicts of interest.

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131 Fig 1 Immediate post-operative x rays-AP View



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133 Fig 2- Immediate post-operative x rays-Lateral View



136 Fig 3-Lateral View of left Knee

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# 138 Microbiological investigations: Table 1 showing Culture results

DATE	TEST	SAMPLE NUMBER	LRN NUMBER	RESULT
13-11-2014	WOUND SWAB- RIGHT LEG C& S	JN-2425	110781	SALMONELLA TYPHI- MODERATE GROWTH SENSITIVE- Ceftriaxone, Ciprofloxacin, Nalidixic acid, Cotrimoxazole, Cefotaxime, Ampicillin, Levofloxacin
15-11-2014	OTHERS C& S	JN-2437	111520	SALMONELLA TYPHI- SCANTY GROWTH SENSITIVE- Ceftriaxone, Ciprofloxacin, Nalidixic acid, Cotrimoxazole, Cefotaxime, Ampicillin, Levofloxacin
	OTHERS C& S	JN-2438	111546	SALMONELLA TYPHI- SCANTY GROWTH SENSITIVE- Ceftriaxone, Ciprofloxacin, Nalidixic acid, Cotrimoxazole, Cefotaxime, Ampicillin, Levofloxacin
17-11-2014	WIDAL TEST	JN-598	11981	TO- 1:160 POSITIVE TH- 1:5120 POSITIVE AH -<1:20 NEGATIVE BH - <1:20 NEGATIVE
20-11-2014	STOOL C& S	JN-2487	113333	NO PATHOGENIC ORGANISM ISOLATED

22-11-2014	WOUND SWAB	JN-2503	114235	NO GROWTH
25-11-2014	WOUND SWAB-	JN-2526	115152	NO GROWTH
	RIGHT LEG			
	WOUND SWAB-	JN-2527	115152	NO GROWTH
	LEFT LEG			
13-12-2014	WIDAL TEST	JN-639	26090	TO- 1:40 NEGATIVE
				TH- 1:320 POSITIVE
				AH -<1:20 NEGATIVE
				BH - <1:20 NEGATIVE
12-1-2014	STOOL C& S	JN-124	BNR	NO PATHOGENIC
				ORGANISM ISOLATED



142 Fig.4 Knee range of movements at 12 weeks follow up.



- 149 Fig.5 Healed surgical wound.



Fig 6. Had episode of infection 3 years after change of poly and debridement-

underwent spacer placement 



- 160 Fig 7-Following placement of final implant

## **Bibliography:**

- 167 1. Peersman G, Laskin R, Davis J, Peterson M. Infection in total knee replacement: a
- 168 retrospective
- review of 6489 total knee replacements. *Clin Orthop.* 2001; 392:15-23.
- 171 2. Wymenga AB, van Horn JR, Theeuwes A, Muytjens HL, Slooff TJ. Perioperative factors

172	associated with septic arthritis after arthroplasty. Prospective multicenter study of			
173	362 knees and 2,651 hip operations. Acta Orthop Scand. 1992; 63:665-671.			
174				
175	3. Trousdale RT, Hanssen AD. Infection after total knee arthroplasty. <i>Instruct Course Lect</i> .			
176	2001; 50:409-414.			
177				
178	4. Nelson CL. Primary and delayed exchange for infected total knee arthroplasty. Am J			
179	<i>Knee Surg.</i> 2001; 14:60-64.			
180				
181	5. Whiteside LA. Treatment of infected total knee arthroplasty. <i>Clin Orthop</i> . 1994;			
182	299:169-172.			
183	6. Goldenberg DL, Cohen AS. Acute infectious arthritis: a review of patients with			
184	nongonococcal			
185	joint infections (with emphasis on therapy and prognosis). Am J Med. 1976; 60:369-377.			
186				
187	7. Sebastian S, Dhawan B, Malhotra R, Gautam D, Kapil A.Salmonella typhimurium			
188	infection in total knee arthroplasty: A case report with review of literature.			
189	J Lab Physicians. 2017 Jul-Sep;9(3):217-219. doi: 10.4103/0974-2727.208254.			
190				
191	8. Rajgopal A, Panda I, Gupta A. Unusual Salmonella typhi periprosthetic joint infection			
192	involving bilateral knees: management options and literature review			
193	BMJ Case Rep. 2017 Nov 14;2017. pii: bcr-2017-221221. doi: 10.1136/bcr-2017-221221.			
194	Review			
195				
196	9. Sánchez-Vargas FM, Abu-El-Haija MA, Gómez-Duarte OG. Salmonella infections: an			
197	update on epidemiology, management, and prevention. Travel Med Infect Dis			
198	2011; 9:263–77.			
199				
200	10. Khan MI, Ochiai RL, von Seidlein L, et al. Non-typhoidal Salmonella rates in febrile			
201	children at sites in five Asian countries. Trop Med Int Health 2010; 15:960–3.			
202				
203	11. Hedberg CW, White KE, Johnson JA, et al. An outbreak of Salmonella enteritidis			
204	infection at a fast-food restaurant: implications for food handler-associated transmission. J			
205	Infect			
206	Dis. 1991; 164:1135-1140.			
207				
208	12 Saphra I, Winter JW. Clinical manifestations of salmonellosis in man: an evaluation of			
209	///9 numan infections identified at the New			
210	York Salmonella Center. N Engl J Med. 1957; 256:1128-1134.			
211				
212	13. Gupta A, Berbari EF, Osmon DR, et al. Prostnetic joint infection due to Salmonella			
213	species: a case series. BMC infect Dis 2014; 14:633.			
214	14 Andrews III Arden CD Hart CM Owen IW Deen infection often total his replacement			
215	14. Andrews HJ, Arden GP, Hart GM, Owen JW. Deep Infection after total nip replacement.			
216	J Bone Joini Surg Br. 1981; 05:55-57			
21/	15 Musanta DB. Orden Salmanella Outhonadica, 2004 Inter27/71.770.2			
218	15. Musanie DB. Oguen SaimonenaOrinopeuics. 2004 Jul;27(7):770-2.			
212	16 Lowenstein MS. An outbrook of colored lines proposed diversion to server			
220	10. Lowenstein MS. An outbreak of samonenosis propagated by person-to-person			
221	transmission on an Indian reservation. Am JEpidemiol. 1975; 102:257-262.			

- 222 17. Threlfall EJ. Antimicrobial drug resistance in Salmonella: problems and perspectives in
- food- and water-borne pathogens. *FEMS*
- 224 *Microbiol Rev.* 2002; 26:141-148
- 18. Davis N, Curry A, Gambhir AK, et al. Intraoperative bacterial contamination in
- 226 operations for joint replacement. *J Bone*
- 227 Joint Surg Br. 1999; 81:886-889
- 19. al-Salem AH, Ahmed HA, Qaisaruddin S, al-Jam'a A, Elbashier AM, al-Dabbous I.
- Osteomyelitis and septic arthritis in sickle cell disease in the eastern province of Saudi
  Arabia. *Int Orthop.* 1992; 16:398-402.
- 231
- 232 20. Cohen JI, Bartlett JA, Corey GR. Extra-intestinal manifestations of *Salmonella* infections.
   233 *Medicine (Baltimore)*. 1987; 66:349-388.
- 234 21. Hohmann EL. Nontyphoidal salmonellosis. *Clin Infect Dis.* 2001; 32:263-269
- 235 236
- 237 22. John J, Van Aart CJ, Grassly NC. The Burden of Typhoid and Paratyphoid in India:
- 238 Systematic Review and Meta-analysis. PLoS Negl Trop Dis 2016;10: e0004616.
- 239
- 240 23.Pachore JA, Vaidya SV, Thakkar CJ, et al. ISHKS joint registry: A preliminary report.
- 241 Indian J Orthop 2013; 47:505–9.
- 242
- 243 244
- 245
- 246 247
- 247
- 249
- 250 251