A retrospective review of gram-negative spinal infections in a single tertiary spinal centre over six years

From Sheffield Teaching Hospitals, Sheffield, UK

D. Tadross,[1,2,3] C. McGrory,[1,4] J. Greig,[1] R. Townsend,[1] N. Chiverton,[1] A. Highland,[1] L. Breakwell,[1] A. A. Cole[1]

[1]Sheffield Teaching Hospitals, Northern General Hospital, Sheffield, UK
[2]Mid-Cheshire Hospitals Trust, Leighton Hospital, Crewe, UK
[3]Yorkshire & Humber Rotation/Mersey Rotation, Sheffield/Liverpool, UK
[4]Yorkshire & Humber Rotation, Sheffield, UK

Correspondence should be sent to D. Tadross d.tadross@nhs.net

Cite this article:
Bone Jt Open 2024;5(5):
435–443.

DOI: 10.1302/2633-1462.55.BJO-2024-0001.R1

Aims

Gram-negative infections are associated with comorbid patients, but outcomes are less well understood. This study reviewed diagnosis, management, and treatment for a cohort treated in a tertiary spinal centre.

Methods

A retrospective review was performed of all gram-negative spinal infections (n = 32; median age 71 years; interquartile range 60 to 78), excluding surgical site infections, at a single centre between 2015 to 2020 with two- to six-year follow-up. Information regarding organism identification, antibiotic regime, and treatment outcomes (including clinical, radiological, and biochemical) were collected from clinical notes.

Results

All patients had comorbidities and/or non-spinal procedures within the previous year. Most infections affected lumbar segments (20/32), with *Escherichia coli* the commonest organism (17/32). Causative organisms were identified by blood culture (23/32), biopsy/aspiration (7/32), or intraoperative samples (2/32). There were 56 different antibiotic regimes, with oral (PO) ciprofloxacin being the most prevalent (13/56; 17.6%). Multilevel, contiguous infections were common (8/32; 25%), usually resulting in bone destruction and collapse. Epidural collections were seen in 13/32 (40.6%). In total, five patients required surgery, three for neurological deterioration. Overall, 24 patients improved or recovered with a mean halving of CRP at 8.5 days (SD 6). At the time of review (two to six years post-diagnosis), 16 patients (50%) were deceased.

Conclusion

This is the largest published cohort of gram-negative spinal infections. In older patients with comorbidities and/or previous interventions in the last year, a high level of suspicion must be given to gram-negative infection with blood cultures and biopsy essential. Early organism identification permits targeted treatment and good initial clinical outcomes; however, mortality is 50% in this cohort at a mean of 4.2 years (2 to 6) after diagnosis.

Take home message

- Gram-negative infection should be considered in older or comorbid patients who present with back pain.
- Biochemical markers alone are not useful indicators of need for surgical intervention.
- Despite positive initial treatment outcomes, gram-negative spinal infection is an indicator of longer-term morbidity and mortalilty.

Bone & Joint Open

Table I. Search terms used in MEDLINE database for literature search.

No.	Term
1	Spine/or spine.mp.
2	Spinal.mp.
3	Vertebral.mp.
4	1 or 2 or 3
5	Discitis.mp. or discitis/
6	Osteomyelitis.mp. or Osteomyelitis/
7	5 or 6
8	Gram-negative bacteria/or gram-negative bacterial infections/or *Escherichia coli*/ or *Pseudomonas aeruginosa*/ or gram-negative.mp.
9	4 and 7 and 8

Introduction

Prompt diagnosis and treatment for spinal infection is essential due to the potentially devastating sequelae of epidural abscess with neurological compromise that can be irreversible, as well as bone destruction with deformity, pain, and/or neurological compromise. Case series have demonstrated that in the majority of cases *Staphylococcus aureus* is isolated as the causative organism.[1,2] However, a significant proportion of infections are caused by gram-negative organisms,[2,3] and the number of these is increasing.[4] Risk factors include age, malignancy, and concurrent infections associated with frailty, such as urinary tract infection.[5] Making a diagnosis and isolating the causative organisms can be complex, with patients often having a background of comorbidity with vague constitutional symptoms a predominant presentation.[6]

Organism isolation is typically achieved by blood culture and/or biopsy, but success is lower in gram-negative infection.[7] However, it has been suggested that gram-negative infections also have a lower rate of progression to epidural or paravertebral abscess.[5] Inflammatory markers have been used as prognostic factors once the diagnosis has been made; treatment failure is thought to be rare when markers, such as ESR or CRP, decline by more than 50% within the first month of treatment.[8] However, some studies have suggested that in multiresistant gram-negative spinal infections inflammatory markers can remain low, making diagnosis more challenging.[9]

There are currently no standardized treatment guidelines for spinal infection, in part due to the small sample sizes collected in the relevant literature. Currently, neurological deficit and mechanical instability are used as significant indicators for surgical management; attempts have also been made to produce clinical-radiological classifications to guide decision-making, but with no clear consensus.[10]

Although there have been a number of retrospective case series of spinal infections (including vertebral osteomyelitis, spondylodiscitis, and epidural abscess), there have been relatively few looking at gram-negative infection specifically. Therefore, our understanding of the diagnostic pathway and patient outcomes for this group specifically is lacking. This study sought to retrospectively analyze gram-negative infections, excluding surgical site infections, in a single tertiary spinal centre (Sheffield Teaching Hospitals, UK) looking at method of diagnosis, antibiotic treatment regimes, surgical intervention, and outcomes, including inflammatory markers and imaging. Following an extensive literature review, the authors believe this is the largest published cohort of gram-negative spinal infections.

Methods

Literature search

A thorough literature search of the MEDLINE database was performed to identify any publications reviewing gram-negative spinal infection. The search terms are outlined in Table I. This produced 183 abstracts which were filtered by one of the authors (AC), leaving 45 abstracts relevant to this published study. The largest case series of gram-negative infections (excluding vertebral osteomyelitis alone and iatrogenic-only series) was 17 patients.[6]

Patient identification

Sheffield Teaching Hospitals has regional tertiary departments in infectious diseases, orthopaedics, and neurosurgery, each caring for patients with spinal infection. Records between 2015 and 2020 inclusive were reviewed for gram-negative spinal infections by searching the monthly spinal infection multidisciplinary team (MDT) patient lists (where all actively treated cases are listed), and from a list of all gram-negative spinal tissue culture samples over the same period. Electronic notes, MDT outcomes, blood, and microbiology investigation were reviewed. One of the authors (AAC) reviewed imaging for all patients. The imaging was classified according to the Spinal Instability Spondylodiscitis Score (SISS),[11] with additions from the classification of Pola et al[10] for abscess formation.

All patients with spinal infection on imaging with a gram-negative organism on blood culture or tissue sample were included in the study. Patients presenting with relapse of previous infection or with infection at the same site of previous surgery were excluded.

Infection characteristics

Data were collected, including vertebral level, extent of infection, past medical history, previous procedures, neurological deficit, treatment regime, inflammatory markers, and outcome. Any antibiotic regimen that lasted longer than five days was included in the analysis. Outcomes were defined as follows: recovered – no further symptoms or residual problems; relapsed – symptoms improved but recurred later; improved – symptoms improved but some residual problems; and death – due to any cause. The project was approved by the local clinical effectiveness department. Ethical approval was not required.

Results

Patient demographics and infection characteristics

In all, 39 patients were initially identified; two patients were identified from microbiology results, but did not have available notes, while five had incomplete documentation regarding antibiotic regimen and treatment outcome due to failed historical note transfer to IT systems. A total of 26/32 patients presented with a main symptom of back pain, with five being generally unwell with pyrexia and one with

Table II. Patient Charlson Comorbidity Index scores and associated short-term treatment and long-term mortality outcomes.

CCI score (with predicted 10-yr survival, %)	Short-term outcome, n				Long-term mortality (2 to 6 yrs post-diagnosis), n	
	Improved	Relapsed	Recovered	Died	Alive	Died
1 (96)	1	2	1	0	3	1
2 (90)	0	0	3	0	3	0
3 (77)	1	1	4	0	3	3
4 (53)	2	0	3	0	3	2
5 (21)	3	0	1	0	1	3
6 (2)	0	1	2	1	1	3
7 (0)	1	0	1	1	2	1
8 (0)	0	0	1	1	0	2
11 (0)	1	0	0	0	0	1
Total					16	16

CCI, Charlson Comorbidity Index.

Table III. Organisms isolated in gram-negative cases of spinal infection.

Organism	Frequency, n (%)
Escheria coli alone	18 (56.3)
Pseudomonas spp.	2 (6.3)
Proteus spp.	2 (6.3)
Bacteroides spp.	2 (6.3)
Haemophilus influenzae	2 (6.3)
Klebsiella pneumoniae alone	2 (6.3)
Klebsiella sp. and *E. coli*	2 (6.3)
Neisseria spp.	1 (3.1)
Pseudomonas spp. and Klebsiella spp.	1 (3.1)

Table IV. Reasons for antibiotic changes for each patient during treatment course.

Reason for antibiotic change	Number
Clinical improvement/appropriate sensitivity (includes IV to oral switch)	16
Remained on same course throughout treatment	6
Outpatient IV antibiotics	5
Lack of clinical improvement/deterioration	2
Allergy and clinical improvement/appropriate sensitivity	1
Renal dysfunction	1
No antibiotic change as died during initial course	1
Total	32

IV, intravenous.

hip pain. Overall, 20/32 patients (62.5%) were male, and the median age at presentation was 71 years (interquartile range (IQR) 60 to 78). A total of 31/32 patients had significant comorbidities, most commonly urological problems and diabetes (each in 31% of patients). Patients scored between 1 to 11 on the Charlson Comorbidity Index;[12] a score of 6 and above indicates a predicted ten-year survival of 2% (see Table II). Overall, 16 patients were alive at the time of data collection (mean 4.2 years post-diagnosis; range 2 to 6).

The lumbar spine was the most commonly affected region (20/32), followed by thoracic (12/32), cervical (3/32), and sacral (2/32). Among the cases, 13 patients had epidural or infected haematoma collections, three had facet joint infection, and seven had paraspinal collection. The most commonly isolated organism was *Escheria coli* alone in over half of cases (17/32; 53.1%) The proportions of other organisms were largely similar to each other (see Table III). Four patients had undergone a surgical procedure within the 12 months prior to diagnosis; two urological, one orthopaedic (intramedullary nailing), and one abdominal surgery. Two patients had historically had spinal surgery at different sites than that of their infection.

Organism isolation and antibiotics selection

All patients had blood cultures taken on admission. This led to organism identification in 23 patients, with two patients having positive organism identification by intraprocedural operative sampling. Seven patients went on to have biopsies/imaging guided aspiration, all of whom had positive organism identification on first biopsy (Figure 1). This study only includes microbiologically proven gram-negative infections, so does not include patients who had no organism identified.

In all, 27 patients had a course of intravenous (IV) antibiotics initially, while five were treated solely with an oral (PO) course; in two cases, early organism and sensitivity identification permitted early use of ciprofloxacin with good

Table V. Radiological review, classified according to the Spinal Instability Spondylodiscitis Score,[11] with additions from the classification of Pola et al[10] for abscess formation.

Levels, n	Location (=frequency)	Bone lesion (=frequency)	Alignment (=frequency)	Epidural collection (=frequency)	Paraspinal collection (=frequency)	Facet infection (=frequency)
		0 = 7		No = 14		
	1 = 8	1 = 4		Small = 7	None = 19	
	2 = 9	2 = 4	0 = 16	Large, non-compressive = 1	Non-drainable = 3	No = 21
Single (n = 23)	3 = 6	4 = 8	2 = 7	Large, compressive = 1	Drainable = 1	Yes = 2
		0 = 2				
	1 = 1	1 = 2	0 = 5	No = 5	None = 6	
Or 3-level contiguous	2 = 3	2 = 1	2 = 2	Small = 2	Non-drainable = 0	No = 7
(n = 8)	3 = 4	4 = 3	4 = 1	Large, non-compressive = 1	Drainable = 2	Yes = 1
Multiple non-contiguous (n = 1)	1 = 1	4 = 1	2 = 1	Small = 1	Non-drainable = 1	No = 1
		0 = 9		**No = 19**		
	1 = 10	**1 = 6**	**0 = 21**	**Small = 10**	**None = 25**	
	2 = 12	**2 = 5**	**2 = 10**	**Large, non-compressive = 2**	**Non-drainable = 4**	**No = 29**
All	**3 = 10**	**4 = 12**	**4 = 1**	**Large, compressive = 1**	**Drainable = 3**	**Yes = 3**
				Location:	**Epidural collection**	
				0 = S2-5	0 = no	
				1 = T3-10	1 = small	
				2 = C3-6; L2-4	2 = large, non-compressive	
				3 = C0-2; C7-T2; T11-L1; L5-S1	3 = large, compressive	
				Bone lesion		
				0 = Disc involvement only		
				1 = Endplate destruction	**Paraspinal collection**	
				2 = < 50% vertebral body destruction	0 = none	
				4 = > 50% vertebral body destruction	1 = small, non-drainable	
					2 = large, drainable	
				Alignment		
				0 = normal		
				2 = denovo deformity (kyphosis/scoliosis)	**Facet joint infection**	
				4 = Subluxation/translation	0 = no	
					1 = yes	

Please refer to the key under the table to identify values for location, bone lesion, and alignment.
SISS, Spinal Instability Spondylodiscitis Score.

effect, and in three cases mild radiological findings and inflammatory marker decrease permitted outpatient management with these patients recovering fully. The shortest course was six weeks, the longest 24 weeks, while the majority of patients (24/32) were treated for 12 weeks. Many patients had courses of more than one antibiotic with a total of 56 regimens in the 32 patients. The most popular antibiotic regimens were PO ciprofloxacin (13/56; 17.6%), IV meropenem (7/56; 9.5%), and PO amoxicillin (3/56; 4.1%). Reasons for extended treatment included stagnant inflammatory markers and development of concurrent infections. Antibiotic changes were due to development of sepsis, concurrent infection, resistance, renal dysfunction, adverse drug reactions, and on conversion from IV to oral, usually at six weeks (Table IV).

Imaging

Overall, 23 patients had single-level discitis, eight had two- or three-level contiguous discitis, and one had two-level discitis in different parts of the spine (see Table V).

There were 12 patient infections (37.5%) with > 50% vertebral body destruction. There were 13 patients (40.6%) with epidural collections, of which three required drainage for neurological deficit, as well as seven (21.9%) with paraspinal collections (Figure 2), three of which were drained radiologically. There were three (9.4%) with facet joint infections on MRI, with one patient just having facet joint infection, but with no epidural collection.

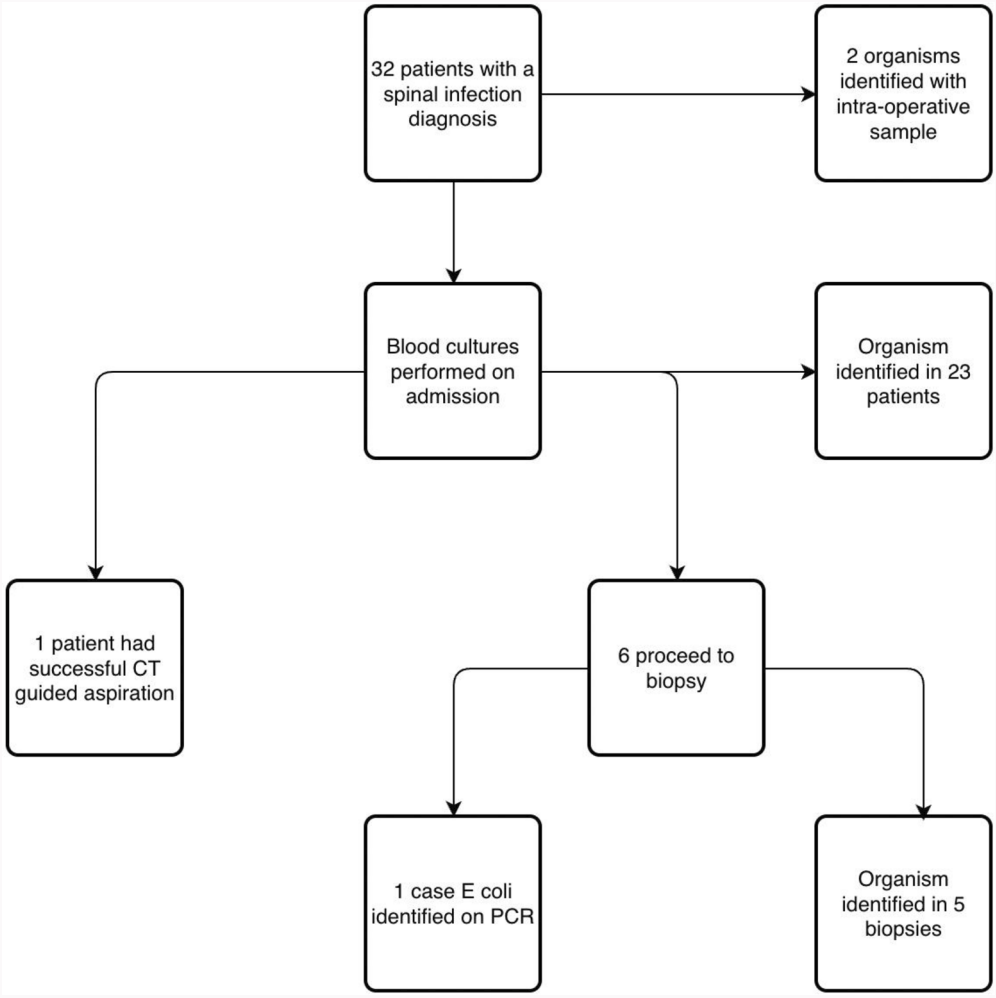

Fig. 1
Organism identification pathway. PCR, polymerase chain reaction.

Inflammatory markers

Mean white cell count (WCC) at start of treatment was 12.9 (standard deviation (SD) 5.3), and mean end of treatment WCC was 8.0 (SD 3.1). Mean CRP at start of treatment was 167.1 (SD 90.1) and 14.2 at the end of treatment (SD 7.3). It took between two to 24 days for the CRP to decrease by 50% with a mean time of 8.5 days (SD 6). It took a mean of 46.7 days (range 9 to 105) for the CRP to normalize.

Surgical interventions and outcomes

Five patients had operative interventions (see Table VI); four had posterior stabilization (two of whom also had decompression), and one had anterior cervical decompression and washout.

Timings of procedures

One operation was performed acutely (within 48 hours of admission) due to neurological deterioration caused by epidural abscess formation (new arm weakness). The patient had anterior cervical decompression (no instrumentation); they recovered from their infection, with resolution of paraesthesia and normal power in all four limbs at final clinic review, with the exception of weakened grip strength in the left hand.

Four patients had sub-acute procedures (more than 48 hours after admission but performed acutely due to clinical change during admission). Two had posterior instrumentation and decompression for an increasing epidural abscess with new neurological deterioration, one had posterior instrumentation and decompression for bony collapse, while one had posterior instrumentation for instability pain.

In patients requiring surgical intervention, the mean initial CRP was lower than in non-surgical patients (158.5 vs 168.6). A 50% reduction in CRP was seen in a shorter period of time following surgery (6.4 days vs 8.4). In both groups, the final CRP resolved to similar levels (11.6 in surgical group vs 14.2 in non-surgical).

Overall, 16 patients recovered from their spinal infection, nine patients improved, and four had relapse of symptoms. There were three deaths during active treatment; one due to stroke, one due to sepsis, and one for which documentation of cause was missing. At 12 months post-diagnosis, six patients (18.8%) had died. At longer-term follow-up (two to six years), this rose to 16 patients (50%), although cause of death was not collected. The mean age of the patients who had died would have been 72.7 years (52 to 92) at the time of data collection; the mean age of the survivors was 70.8 years (55 to 85).

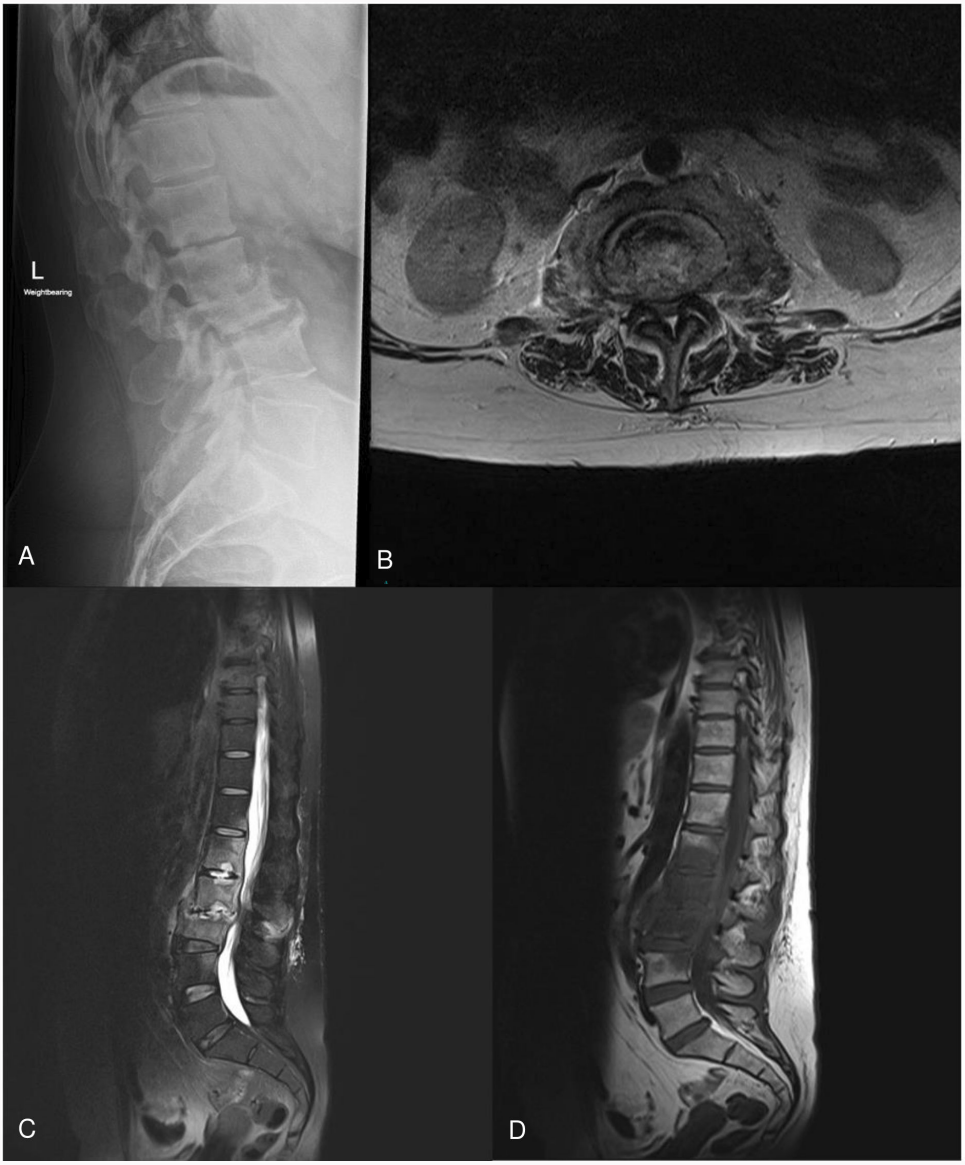

Fig. 2
a) Lateral lumbar spine radiograph showing L2/3 discitis with L2/3 disc space destruction, less than 50% destruction of L3 and mild inferior endplate of L2 destruction. There is mild endplate destruction at L3/4. b) Axial T2 image shows epidural and paraspinal abscesses. c) to d) Inflammatory tissue in the paraspinal region. Inflammation in the right psoas, which can progress to a psoas abscess. T2 and T1 sagittal MRI imaging shows disc space destruction and fluid collections such as epidural abscess. d) T1 imaging shows the true extent of the vertebral body involvement extending up into L1 and down into L4.

Discussion

This study sought to review the investigation, management, and outcomes of gram-negative spinal infections. In all, 24/32 patients (75%) recovered or improved, representing a high treatment success rate in a clinically vulnerable population. However, 18.8% of patients were deceased 12 months post-diagnosis and 50% were deceased at a mean of 4.2 years (range 2 to 6 years). This is indicative of longer-term problems in a similar way to neck of femur and odontoid peg fractures. These fragility fractures are considered markers of poor prognosis associated with a 33% and 34.1% mortality at one year, respectively.[14,15] A diagnosis of gram-negative infection in the elderly should be taken similarly seriously. Gram-negative infection is already associated with poor outcomes in other orthopaedic subspecialities.[16] A substantial Danish cohort study has found increased short- and long-term mortality in spondylodiscitis patients relative to a control group, due to both disease burden and patient social/health behaviours.[17] In a cohort of 183 undifferentiated discitis cases, mortality was 28% at a median point of 68 months.[18] Exact long-term prognosis beyond treatment completion is not clear, but evidence suggests spinal infection has a deleterious effect on future health. The findings of our study suggest that gram-negative spinal infection is a compounding negative prognostic sign and may be indicative of reduced life expectancy, potentially akin to major traumatic injuries such as neck of femur fracture. Whether this is due to pre-existing comorbidity, or the morbidity associated with infection of a significant body-system and extended treatment, is not entirely clear, but the association is evident.

Due to the study design, all patients had a microbiological diagnosis of gram-negative spinal infection, so it is

Table VI. Patients who had operations during admission.

Age, sex	Diagnosis	Microbiology	Neurological dysfunction	Indication for surgery	Operative intervention	Operated acutely (within 48 hrs of admission) or subacutely	Outcome	Alive at time of review
60 M	C5/6 T8/9 discitis	*Escheria coli* in blood cultures	Nil	Pain and instability	Posterior T6-T11 instrumented stablization	Sub-acute	Recovered	No
49 F	T8/9 discitis with small epidural abscess	*E. coli* in blood cultures	ASIA D[13]	New left leg weakness	Posterior thoracic stablization and decompression	Sub-acute	Improved	No
82 F	T9/10 discitis	*E. coli* in blood cultures	ASIA C[13]	Unspecified neurological deterioration	T9/10 decompression and posterior stablization for abscess	Sub-acute	Improved	Yes
55 M	C5/6 epidural collection	*Haemophilus parainfluenzae* in theatre samples	ASIA D[13]	New arm weakness	C5/6 anterior cervical decompression and washout	Acute	Improved	Yes
65 F	T6-9 discitis	*Klebsiella pneumoniae/E. coli* in blood cultures	Nil	Bony collapse	Posterior T3-T11 instrumented stablization	Sub-acute	Relapsed	No

ASIA, American Spinal Injury Assocation.

not possible to evaluate the rate of positive blood cultures or biopsy. However, 23/32 patients (71.9%) were diagnosed with blood culture, 6/32 (18.8%) with biopsy, and 3/32 (9.4%) from intraoperative/image-guided aspiration samples. Previous studies have suggested a positive blood culture rate of 56% to 72%,[6,19] and positive image-guided biopsy rate of 31% to 91% with a recent meta-analysis suggesting a yield of 48%.[20] Where blood cultures were negative, the use of biopsy permitted targeted antibiotic treatment for these patients where empirical antibiotics would be an inferior solution. The Infectious Diseases Society of America advises percutaneous biopsy only in cases with negative blood cultures,[21] which is our local policy. Previously concordance of 89% has been found between blood culture and biopsy organism findings, and in the same study only in 3/97 patients did biopsy lead to antibiotic changes to cover previously unidentified organisms.[22] Biopsy has the potential to yield useful clinical information where organism identification has failed, but in many cases blood culture is sufficient to rationalize antibiotic regimes.

Gram-positive organisms traditionally predominate as the causative agent in spinal infection. A previous study from our centre showed that 32/39 patients (82%) with *S. aureus* discitis recovered or improved from infection,[23] which is comparable to 24/32 (75%) in this study. Overall, 18% of those gram-positive patients required surgical intervention, similar to the 15.6% in this gram-negative population. Of note, it appeared to be more difficult to rationalize antibiotics in gram-negative cases, with 56 different treatment regimes used. The association of gram-negative infection and comorbidity, seen in the literature with older patients who have a higher incidence of malignancy and concurrent illness,[6] is borne out in our data. Only one patient in the study had no known long-term medical problems.

The regional distribution of infection, with a predominance in the lumbar spine, is comparable to the previous paper from our centre on *S. aureus* spinal infection.[23] It has been suggested that gram-negative infections tend less towards progressing to collection or epidural abscess. Our study found epidural abscess in 13 cases (40.6%) as opposed to 73% in a series of gram-positive spinal infections,[6] and 28% in a previous series of gram-negative spinal infections.[5] Furthermore, only in three patients was drainage clinically indicated. Therefore, it appears that while the frail and immunosuppressed are more vulnerable to gram-negative spinal infection, their rate of abscess formation and progression beyond discitis is reduced. Gram-negative spinal infection should be considered in frail or immunosuppressed patients who present with back pain.

Neurological deficit, ranging from radicular pain to limb weakness, is reported in 12/32 patients (37.5%) in our cohort, which is similar to a previous study, where 15/46 discitis (staphylococcus and tuberculous organisms) patients presented with symptoms, including paraesthesia and weakness.[19] Given the seemingly lower rate of abscess formation in gram-negative infection,[5,6] an equal or lesser neurological burden than in gram-positive could be anticipated.

The majority of infections were treated with a 12-week course of antibiotics, in keeping with contemporary literature and practice.[24–26] Five patients were treated with only PO antibiotic regimes as, for example, ciprofloxacin, an antibiotic which has good efficacy when taken orally. Four of these patients recovered and one patient improved, with no relapses recorded. Notably, each of these patients had simple discitis with no neurological symptoms, demonstrating that patient selection is important, with early organism and sensitivity identification. They were mainly patients who remained ambulatory. Antibiotic selection was made in liaison with microbiology and infectious disease specialists in the regular local spinal infection MDT meeting based on organism and culture sensitivities. The case where a patient had

24 weeks' of antibiotics was due to concurrent infections in an immunocompromised patient, demonstrating the susceptibility of patients who are vulnerable to gram-negative infection to other complications.

Admission CRP was lower in operated patients, which suggests that biochemical markers alone are not accurate predictors of need for surgery with decision-making based on the clinical assessment, such as neurological symptoms or bone destruction. While previous evidence suggests that a drop in ESR of 50% within the first month suggests likely treatment success, our study demonstrates that the mean time for this drop to occur in CRP is 8.5 days (SD 6) in a cohort where 24/32 patients at least improved. A mean decrease taking longer than 20 days (mean + 2SDs) may suggest a risk of treatment failure.

As previously published, *E. coli* was the most prevalent gram-negative organism, found in 56.3% of cases compared to 35% in the previously largest series identified in a literature search.[6] The next most prevalent organisms identified included proteus, bateroides, klebsiella, and haemophilus species with no predominance of any specific bacteria, similar to the Lee et al[6] study.

Limitations

The authors acknowledge that the number of cases highlighted in this paper reflects the low incidence of gram-negative spinal infection, but, to the authors' knowledge, does also constitute the largest published case series. As the data were retrospectively collected, where information was unavailable, patients had to be excluded, and in some circumstances details were incomplete. As a tertiary centre receiving referrals, patients' initial blood tests were merely those during treatment at our hospital and may not in each case represent the point of initial diagnosis. In many cases where patients were deceased, it was not possible to ascertain their cause of death and therefore understand the specific link, if any, to their spinal infection. It should also be acknowledged that as this data was collected in late 2021, the COVID-19 pandemic may have contributed as a confounder, increasing the number of deaths among this patient cohort, as they represent the clinically vulnerable population at increased risk of death from the virus.

In conclusion, although associated with comorbidity, early identification of organisms in gram-negative spinal infection permits targeted treatment and good initial clinical outcomes. In most cases blood cultures are sufficient, but image-guided biopsy has a high yield and should be performed where no organism is identified on blood culture. Surgical management is indicated by clinical findings rather than objective measures. Despite treatment success, gram-negative infection appears to be associated with high short- to medium-term mortality.

References

1. **Kim UJ**, **Bae JY**, **Kim S-E**, **et al**. Comparison of pyogenic postoperative and native vertebral osteomyelitis. *Spine J*. 2019;19(5):880–887.
2. **Fransen BL**, **de Visser E**, **Lenting A**, **Rodenburg G**, **van Zwet AA**, **Gisolf EH**. Recommendations for diagnosis and treatment of spondylodiscitis. *Neth J Med*. 2014;72(3):135–138.
3. **Nolla JM**, **Ariza J**, **Gómez-Vaquero C**, **et al**. Spontaneous pyogenic vertebral osteomyelitis in nondrug users. *Semin Arthritis Rheum*. 2002;31(4):271–278.
4. **Graham SM**, **Fishlock A**, **Millner P**, **Sandoe J**. The management gram-negative bacterial haematogenous vertebral osteomyelitis: a case series of diagnosis, treatment and therapeutic outcomes. *Eur Spine J*. 2013;22(8):1845–1853.
5. **Park K-H**, **Cho OH**, **Jung M**, **et al**. Clinical characteristics and outcomes of hematogenous vertebral osteomyelitis caused by gram-negative bacteria. *J Infect*. 2014;69(1):42–50.
6. **Lee C-Y**, **Wu M-H**, **Cheng C-C**, **et al**. Comparison of gram-negative and gram-positive hematogenous pyogenic spondylodiscitis: clinical characteristics and outcomes of treatment. *BMC Infect Dis*. 2016;16(1):735.
7. **Amsilli M**, **Epaulard O**. How is the microbial diagnosis of bacterial vertebral osteomyelitis performed? An 11-year retrospective study. *Eur J Clin Microbiol Infect Dis*. 2020;39(11):2065–2076.
8. **Carragee EJ**, **Kim D**, **van der Vlugt T**, **Vittum D**. The clinical use of erythrocyte sedimentation rate in pyogenic vertebral osteomyelitis. *Spine (Phila Pa 1976)*. 1997;22(18):2089–2093.
9. **Shiban E**, **Janssen I**, **Wostrack M**, **et al**. Spondylodiscitis by drug-multiresistant bacteria: a single-center experience of 25 cases. *Spine J*. 2014;14(12):2826–2834.
10. **Pola E**, **Autore G**, **Formica VM**, **et al**. New classification for the treatment of pyogenic spondylodiscitis: validation study on a population of 250 patients with a follow-up of 2 years. *Eur Spine J*. - 2017;26(Suppl 4):479–488.
11. **Schömig F**, **Li Z**, **Perka L**, **et al**. Georg schmorl prize of the German spine society (DWG) 2021: Spinal Instability Spondylodiscitis Score (SISS)-a novel classification system for spinal instability in spontaneous spondylodiscitis. *Eur Spine J*. 2022;31(5):1099–1106.
12. **Charlson ME**, **Pompei P**, **Ales KL**, **MacKenzie CR**. A new method of classifying prognostic comorbidity in longitudinal studies: development and validation. *J Chronic Dis*. 1987;40(5):373–383.
13. **No authors listed**. American Spinal Injury Association. https://asia-spinalinjury.org/wp-content/uploads/2023/12/ASIA-ISCOS-Worksheet-Sides-12_12_4_2023.pdf (date last accessed 10 May 2024).
14. **Moran CG**, **Wenn RT**, **Sikand M**, **Taylor AM**. Early mortality after hip fracture: is delay before surgery important? *J Bone Joint Surg Am*. 2005;87-A(3):483–489.
15. **Shafafy R**, **Valsamis EM**, **Luck J**, **et al**. Predictors of mortality in the elderly patient with a fracture of the odontoid process. *Bone Joint J*. 2019;101-B(3):253–259.
16. **Kalbian IL**, **Goswami K**, **Tan TL**, **et al**. Treatment outcomes and attrition in gram-negative periprosthetic joint infection. *J Arthroplasty*. 2020;35(3):849–854.
17. **Aagaard T**, **Roed C**, **Dahl B**, **Obel N**. Long-term prognosis and causes of death after spondylodiscitis: a Danish nationwide cohort study. *Infect Dis (Lond)*. 2016;48(3):201–208.
18. **Stoop N**, **Zijlstra H**, **Ponds NHM**, **Wolterbeek N**, **Delawi D**, **Kempen DHR**. Long-term quality of life outcome after spondylodiscitis treatment. *Spine J*. 2021;21(12):1985–1992.
19. **Perronne C**, **Saba J**, **Behloul Z**, **et al**. Pyogenic and tuberculous spondylodiskitis (vertebral osteomyelitis) in 80 adult patients. *Clin Infect Dis*. 1994;19(4):746–750.
20. **McNamara AL**, **Dickerson EC**, **Gomez-Hassan DM**, **Cinti SK**, **Srinivasan A**. Yield of image-guided needle biopsy for infectious discitis: a systematic review and meta-analysis. *AJNR Am J Neuroradiol*. 2017;38(10):2021–2027.
21. **Berbari EF**, **Kanj SS**, **Kowalski TJ**, **et al**. 2015 Infectious Diseases Society of America (IDSA) clinical practice guidelines for the diagnosis and treatment of native vertebral osteomyelitis in adults. *Clin Infect Dis*. 2015;61(6):e26–46.
22. **Lim E**, **Walter W**, **Gyftopoulos S**, **Samim M**. Does image-guided biopsy of discitis-osteomyelitis provide meaningful information to impact clinical management? *Skeletal Radiol*. 2021;50(7):1325–1336.
23. **Locke T**, **Kell ME**, **Bhattacharyya D**, **Cole AA**, **Chapman ALN**. Spontaneous methicillin-sensitive Staphylococcus aureus spondylodiscitis-Short course antibiotic therapy may be adequate: evidence from a single centre cohort. *J Infect Public Health*. 2014;7(1):44–49.
24. **Skaf GS**, **Domloj NT**, **Fehlings MG**, **et al**. Pyogenic spondylodiscitis: an overview. *J Infect Public Health*. 2010;3(1):5–16.

25. **Aagaard T**, **Roed C**, **Dragsted C**, **Skinhøj P**. Microbiological and therapeutic challenges in infectious spondylodiscitis: a cohort study of 100 cases, 2006-2011. *Scand J Infect Dis*. 2013;45(6):417–424.

26. **Cottle L**, **Riordan T**. Infectious spondylodiscitis. *J Infect*. 2008;56(6):401–412.

Author information

D. Tadross, MBChB, MRes(Med), PGCert(MedEd), MRCS, Core Surgical Trainee/Specialty Registrar,
Sheffield Teaching Hospitals, Northern General Hospital, Sheffield, UK;
Mid-Cheshire Hospitals Trust, Leighton Hospital, Crewe, UK;
Yorkshire & Humber Rotation/Mersey Rotation, Sheffield/Liverpool, UK.

C. McGrory, MBChB, PGCert(MedEd), MRCS, Core Surgical Trainee, Sheffield Teaching Hospitals, Northern General Hospital, Sheffield, UK; Yorkshire & Humber Rotation, Sheffield, UK.

J. Greig, MBBS, BSc, DTM&H, FRCP, Infectious Diseases Consultant
R. Townsend, MBChB, MSc, DTMH, FRCPath, Consultant Medical Microbiologist
N. Chiverton, MBBS, Spinal Surgery Consultant
A. Highland, MB ChB, MRCP, FRCR, Radiology Consultant
L. Breakwell, MBChB, MSc, FRCS (Tr&Orth), Consultant Spinal Surgeon
A. A. Cole, BMedSci, FRCS(Tr&Orth), DM, Spinal Surgery Consultant
Sheffield Teaching Hospitals, Northern General Hospital, Sheffield, UK.

Author contributions

D. Tadross: Conceptualization, Data curation, Formal analysis, Investigation, Methodology, Project administration, Validation, Visualization, Writing – original draft, Writing – review & editing.
C. McGrory: Data curation, Formal analysis.
J. Greig: Methodology, Writing – original draft.
R. Townsend: Data curation, Formal analysis, Writing – original draft.
N. Chiverton: Data curation, Formal analysis, Writing – original draft.
A. Highland: Data curation, Formal analysis, Writing – original draft.
L. Breakwell: Data curation, Formal analysis, Writing – review & editing.
A. A. Cole: Conceptualization, Data curation, Formal analysis, Investigation, Methodology, Project administration, Validation, Visualization, Supervision, Writing – original draft, Writing – review & editing.

Funding statement

The authors received no financial or material support for the research, authorship, and/or publication of this article.

ICMJE COI statement

L. M. Breakwell discloses being an invited speaker to the Stryker Spinal Deformity Course 2023; and holding a leadership or fiduciary role for the British Scoliosis Society, which are unrelated to this paper. A. A. Cole declares being chief investigator for the National Institute for Health and Care Research Health Technology Assessment grant for bracing in adolescent idiopathic scoliosis (NIHR131081); being on the Spinal Expert Advisory board for the Medicines and Healthcare products Regulatory Agency, and member of Spinal ODEP/Beyond Compliance committee; and being past president of the British Scoliosis Society, British Spine Registry Deputy Lead for the British Association of Spine Surgeons, and Spinal Chair for Orthopaedic Expert Working Group for National Casemix Office, all of which are unrelated to this work.

Data sharing

The datasets generated and analyzed in the current study are not publicly available due to data protection regulations. Access to data is limited to the researchers who have obtained permission for data processing. Further inquiries can be made to the corresponding author.

Acknowledgements

The authors would like to thank the Sheffield Teaching Hospitals spinal infection multidisciplinary team for their support.

Ethical review statement

Ethical approval was not required for this study

Open access funding

The authors report that the open access funding for this manuscript from was self-funded.