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Original article

Red flags for spinal pain in patients diagnosed with spinal infection in Nigeria: A 10-year medical records review

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ABSTRACT

Background: Spinal infection is a diagnostic challenge, the personal and economic consequences of misdiagnosis can be significant resulting in paralysis and instability of the spine and can ultimately be fatal. To aid identification of those at risk of spinal infection, a better understanding of the red flags for spinal infection is needed.
Objective: To better understand which red flags may help to identify spinal infection.
Design: and Methods: A 10-year medical records review of red flags for spinal infection in Nigeria, using a bespoke data extraction tool. Univariable and multivariable logistic regression was used to identify the main independent predictors of spinal pain.
Results: 124,913 records were reviewed, 1,645 patients were diagnosed with spinal infection. 79% of patients presented with spinal pain Univariable analysis revealed nine factors (some centres, all age groups above 16 years, co-morbidities, environmental factors, history of TB, radicular pain, pins and needles, numbness and spine tenderness.) were associated with greater odds (OR = 1.77–21.7, $p < 0.001$), whilst four (some centres, fatigue, fever and myotomal weakness) were associated with lower odds (OR = 0.51–0.59) of spine pain. Six factors were included in the final multivariable model associated with higher odds of spine pain: age groups above 16 years (OR 2.57 to 5.33, $p < 0.05$), co-morbidity (OR = 1.68, $p < 0.05$), history of TB (OR = 3.02, $p < 0.05$), weight loss (OR = 1.75, $p < 0.01$), radicular pain (OR = 19.88, $p < 0.001$); spine tenderness (OR = 6.54, $p < 0.001$). Myotomal weakness (OR = 0.66, $p < 0.05$) and fatigue (OR = 0.50, $p < 0.01$) were associated with lower odds of spinal pain in the final model.
Conclusion: Using data from ten hospitals in Nigeria within a ten-year period, we have produced a shortlist of red flags that can inform clinical decision making about potential spinal infection.

1. Background/introduction

In 2017, low back pain was the leading cause of years lived with disability; globally 57.6 million years were lost to disability across 195 countries (GBD collaborators, 2017). Internationally, musculoskeletal practitioners face a daily diagnostic challenge i.e., a small percentage of this large number of patients consulting with back pain have non-musculoskeletal, serious underlying causes for their pain. Budtz et al. (2021) reported the overall prevalence of serious pathology as 2.3% in musculoskeletal physiotherapy patients in Denmark, the prevalence of spinal infection was 0.01%. Spinal infection along with Cauda Equina Syndrome (CES); Spinal Fracture; and Malignancy is one of four

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key serious spinal pathologies of concern to musculoskeletal practitioners (Finucane et al., 2020). This is because spinal infection can progress with serious personal complications such as paralysis, instability of the spine, and can ultimately be fatal (Finucane et al., 2020). In addition to these health consequences, there is also a significant economic burden associated with spinal infection. Therefore, it is vital that musculoskeletal practitioners are equipped to recognise and identify spinal infection cases. However, the diagnosis of spinal infection is challenging and is reported to be a result of two main issues: failure to consider spinal infection as a potential differential diagnosis and failure to recognise the relevant risk factors and clinical features (Patel et al., 2014; Khoriati et al., 2012). In a case report, Greenhalgh and Selfe (2010) highlight a number of the challenges associated with diagnosing spinal infection in a case that took 13 months to diagnose, with the patient having been seen by five different medical specialities through the prodromal period.The global distribution of spinal infection varies considerably. For example, Nigeria has one of the highest TB incidence rates globally with a rate of 219 per 100 000 per population (WHO 2020a); this is 27 times the rate of the United Kingdom. Skeletal TB accounts for 10–20% of all extra-pulmonary TB, with spinal involvement occurring in up to 5% of all TB cases (Schirmer et al., 2010). Extra-pulmonary TB presents with a wide range of symptoms, back pain being the most frequent (Patel et al., 2016). In low resource settings, such as Nigeria, where there is likely to be a relatively high number of spinal infection patients, and access to imaging and other diagnostic testing may be limited, the early identification of spinal infection using clinical red flags is very important. There is concern about the relatively lower treatment success rates and excess mortality rates among extra-pulmonary TB patients in African nations. The importance of vigilance to facilitate early diagnosis to improve treatment outcomes and minimize the risk of progression to advanced forms of disease and death is highlighted as a key goal of many national TB control programmes (Ohene et al., 2019).

In a recent review examining red flags for spinal infection (Yusuf et al., 2019), all papers reviewed originated from either High or Upper Middle-Income countries, where spinal infection is rare, and none from Middle- or Low-Income countries, where spinal infection is much more common. This reporting bias, whereby countries with the largest burden of spinal infection are not represented in the literature, highlights a key weakness in the current evidence base for red flags for spinal infection as our knowledge is based on a relatively small number of cases. The financial costs of misdiagnosing spinal infection are substantial. Even in countries with well-developed healthcare systems, despite being relatively rare, spinal infection ranks as one of the most significant categories of diagnostic errors in primary care. For example, between 2002 and 2010, spinal infection accounted for 11.6% of all spinal-related malpractice litigation in the UK, costing the National Health Service £433,296 per case (Quraishi et al., 2012).

To address the lack of evidence on the red flags for spinal infection in low resource settings, we conducted a medical records review within a ten-year period in ten hospitals in Nigeria to examine red flags for spinal pain in patients with a confirmed diagnosis of spinal infection.

2. Methods

Following local ethical and governance approvals (NOHD/RET/ETHIC/60: ABUTH/HREC/UG/6: NHREC/28/01/2020/AKTH/EC/2816; UI/EC/20/0143), permission to extract data was also obtained from management and heads of physiotherapy departments at the different hospital centres. Data was thereafter extracted from the medical records of 10 hospital centres in 7 different States in the South Western, South Eastern and North Western Regions of Nigeria between 2009 and 2020 (Table 2).

2.1. Case definition

All available records between the years 2009 and 2020 were screened for a diagnosis of TB; *Staphylococcus aureus*; Brucellosis; or other spinal infection (Yusuf et al., 2019) and a report of spinal pain. We extracted data from the medical records using a bespoke 17 item list designed for this study, based on the international framework for red flags for potential serious spinal pathologies (Finucane et al., 2020) (See Table 1).

Data Abstractors. Through a Manchester Metropolitan University Global Challenges Research Fund grant (GCRF/QR: 370356), we employed junior physiotherapists, who were experienced in data extraction, to conduct the data extraction of medical records at each of the 10 hospitals in Nigeria. The abstractors were trained locally at each of the data collection centres by the lead Nigerian investigators. The training included the purpose of the study and how to accurately extract data on the relevant variables from case notes of patients using the bespoke data extraction tool. As part of the quality assurance process, the accuracy of the records of each data abstractor was audited twice weekly by one of the lead Nigerian investigators but formal testing of inter-rater reliability was not conducted.

Missing data. There were eight cases of missing data. Four patients had missing information on age and sex, and four had no information on

Table 1
Information extracted from the records.

Demographics	
Sex	
Age	
Risk Factors	
Co-morbidities and immunosuppression	Diabetes, HIV/AIDS, rheumatoid arthritis, pre-existing infections, long-term use of steroids, Cancer, Cardiovascular disease, Renal failure, Liver disease
Surgery and invasive procedures	Spinal or adjacent areas, spinal injections, revisions
Social factors	Intravenous drug use, alcohol abuse
Environmental factors	Migrant, occupational exposure, homelessness, prisoners, contact with infected animals
History of TB	Has had TB or was born in TB endemic country such as Nigeria, South Africa, Kenya
Recent pre-existing infection	Sepsis, infection, fever
Clinical Features: Patient reported symptoms (subjective)	
Spinal pain	
Radicular pain	
Pins and needles in the lower limbs	
Numbness in the lower limbs	
Weakness in lower limbs	
Fatigue	General or underperforming normal activities
Fever	
Unexplained weight loss	In 3–6 months have lost >5%
Clinical Features: Clinical examination findings (objective)	
Spine tenderness on palpation	
Neurological signs affecting lower limb dermatomes	
Neurological signs affecting lower limb myotomes	
Neurological signs affecting lower limb reflexes	
Investigations	
Observations: HR, BP, Temperature	
Blood tests	
X-rays	
MRI scans	
CT scans	
Other	
Diagnosis and treatment	
What was diagnosis	

Table 2
Data sources: All available records from a 10-year period were screened for a diagnosis of spinal infection.

Institution	Location/ State/ Region	Years reviewed	Number of physiotherapy and/or general out patients records reviewed	Number of Spinal Infection cases with spinal pain
National Orthopaedic Hospital, Igbobi, Lagos (NOHIL)	Lagos, Lagos State, South Western	2009–2019	1907	202
University College Hospital (UCH)	Ibadan, Oyo State, South Western	2009–2019	9020	41
Ladoke Akintola University of Technology Teaching Hospital (LAUTECH)	Osogbo, Osun State, South Western	2010–2020	3525	11
Obafemi Awolowo University Teaching Hospitals Complex (OAUTHC)	Ile-Ife, Osun State, South Western	2010–2020	16,355	64
Nnamdi Azikwe University Teaching Hospital (NAUTH-Oba)	Oba, Anambra State, South Eastern	2011–2020	99	43
Nnamdi Azikwe University Teaching Hospital (NAUTH-Nnewi)	Nnewi, Anambra State, South Eastern	2011–2020	485	65
University of Nigeria Teaching Hospital (UNTH)	Enugu, Enugu State, South Eastern	2011–2020	93	31
National Orthopaedic Hospital, Dala (NOHD)	Kano, Kano State, North Western	2011–2020	67,267	799
Aminu Kano Teaching Hospital (AKTH)	Kano, Kano State, North Western	2010–2019	16,292	232
Ahmadu Bello University Teaching Hospital (ABUTH)	Zaria, Kaduna State, North Western	2010–2020	9870	165
			Total 124,913	**Total 1,653**

the presence of spinal pain, these patients were excluded. The analytic sample was therefore 1,645 patients (see Fig. 1).

2.2. Statistical analysis

The total number of cases recorded with spinal pain and with the variables detailed in Table 1 were determined along with the prevalence rate. Each potential risk factor was initially modelled in a univariable logistic regression with spinal pain (yes vs. no) as the outcome variable to derive the odds ratio (OR), 95% confidence intervals and probability. Then, to avoid ruling out risk factors prematurely based on significance

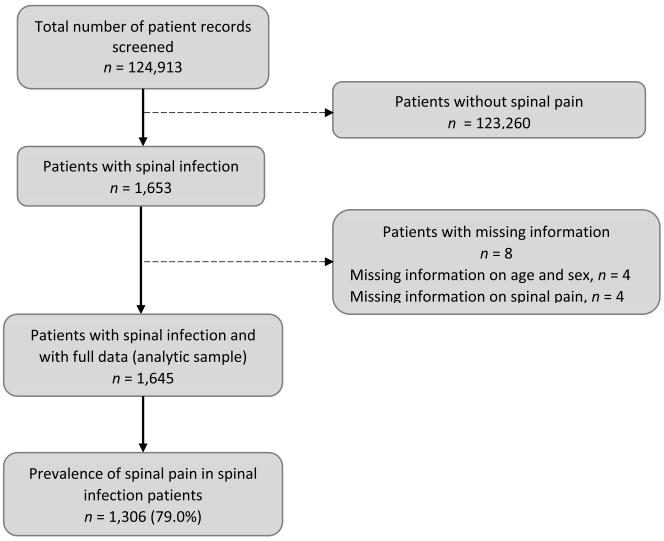

Fig. 1. Flow diagram of spinal infection patients included in the study as well prevalence of spinal pain.

at a univariable level, all factors were then entered into a multivariable model to determine their contribution when adjusting for all other factors (Bullock et al., 2021). Once complete, a backward elimination process took place with factors that resulted in a p value above 0.05 or an OR below 1.30 or an OR above 0.77 (stopping criteria) removed to give a final model (Bullock et al., 2021). This identified the main independent factors associated with spinal pain in the sample. The significance level (2-sided) was interpreted at 0.05 but highlighted as $p < 0.01$ and $p < 0.001$ where applicable. All analyses were performed using Statistic Package Social Sciences Version 27 (SPSS, Armonk, USA).

3. Results

A total of 124,913 case notes were reviewed from 10 centres between 2009 and 2020 (Fig. 1). In this period, there were 1,645 patients diagnosed with spinal infection and who had data available, a prevalence of 1.3%. Of those diagnosed with spinal infection, 1,306 patients (79.0%) reported having spinal pain. Table 2 shows the information on the centre, demographic, and risk factors stratified by the presentation of spinal pain. Amongst the patients diagnosed with spinal infection, the prevalence of spinal pain ranged from 50.9 to 100% across the 10 centres. Across the three models, three centres appear to have much greater odds of spine pain in patients, whereas two centres had much lower odds (Table 3). Compared to those aged 16 years and under, the odds of spinal pain were greater in all other age groups, ranging from 4.17 to 7.64 (Table 3).

Minimal differences were observed in both the prevalence and odds of spinal pain between men and women. The prevalence of spinal pain was 0.8%–12.5% higher in patients that stated they had other co-morbidities, recent surgery or invasive procedures, social factors, environmental factors, numbness, weakness, weight loss and absent reflexes (Table 3). A higher prevalence of spinal pain was observed in those that had a history of TB (82.0%), pins and needles (91.6%), and spinal tenderness (94.2%).

The results from the univariable analysis revealed nine factors that were associated ($p < 0.05$ or OR > 1.30) with an increased odds of spinal pain within this population. These included some centres, all age groups above 16 years, co-morbidities, environmental factors, history of TB, radicular pain, pins and needles, numbness and spine tenderness. Four factors were associated ($p < 0.05$ or OR < 0.77) with reduced odds of spinal pain within this population; these include presenting to some centres, fatigue, fever, and myotomal weakness. The multivariable analysis revealed a total of twelve factors (see Table 3) were associated

Table 3
The relationship between centre, age group and potential risk factors with the likelihood of reporting spinal pain.

Variable	Spinal Pain Yes	Spinal Pain No	Prevalence (%)	Univariable OR (95% CI) Unadjusted	Multivariable OR (95% CI)	Multivariable OR (95% CI) Final Model
Centre						
ABUTH	84	81	50.9	0.24 (0.17, 0.34)***	0.42 (0.23, 0.78)***	0.41 (0.22, 0.74)**
AKTH	175	56	75.6	0.72 (0.51, 1.02)	0.97 (0.58, 1.65)	0.99 (0.60, 1.63)
LAUTECH	11	0	100	–	–	–
NOHIL	197	5	97.5	9.12 (3.69, 22.5)***	19.48 (7.32, 51.81)***	18.06 (6.89, 47.28)***
NOHD	646	150	81.2	*Referent*	*Referent*	*Referent*
NAUTH (Nnewi)	50	15	76.9	0.77 (0.42, 1.42)	2.50 (0.96, 6.53)	2.33 (0.93, 5.84)
NAUTH (Oba)	42	1	97.7	9.72 (1.33, 71.2)*	23.11 (2.67, 200.44)**	21.09 (2.47, 179.87)**
OAUTHC	62	2	96.9	7.20 (1.74, 29.8)**	44.74 (9.36, 213.81)***	37.16 (8.00, 172,56)***
UCH	19	22	46.3	0.20 (0.11, 0.38)***	0.68 (0.27, 1.67)	0.67 (0.29, 1.55)
UNTH	20	11	64.5	0.42 (0.20, 0.90)*	0.32 (0.11, 0.941)*	0.32 (0.11, 0.90)*
Demographics						
Age (years)						
16 and under	63	77	45.0	*Referent*	*Referent*	*Referent*
17-29	280	82	77.3	4.17 (2.76, 6.31)***	3.89 (2.12, 7.16)***	4.04 (2.28, 7.17)***
30-39	223	36	86.2	7.57 (4.66, 12.29)***	5.33 (2.70, 10.55)***	5.33 (2.77, 10.24)***
40-49	208	51	80.3	4.99 (3.17, 7.84)***	2.63 (1.35, 5.12)**	2.57 (1.36, 4.85)**
50-59	239	47	83.6	6.22 (3.94, 9.81)***	4.56 (2.27, 8.76)***	4.44 (2.34, 8.42)***
60–69	181	33	84.6	6.70 (4.07, 11.0)***	3.03 (1.47, 6.28)**	3.09 (1.55, 6.15)**
70 and over	100	16	86.2	7.64 (4.09, 14.3)***	3.55 (1.53, 8.28)**	3.92 (1.75, 8.75)***
Sex						
Men	514	134	79.3	*Referent*		
Women	788	207	79.2	1.01 (0.79, 1.29)	0.91 (0.64, 1.30)	–
Risk Factors						
Co-morbidity						
No	940	281	77.0	*Referent*		
Yes	362	61	85.6	1.77 (1.31, 2.40)***	1.77 (1.14, 2.76)*	1.68 (1.09, 2.58)*
Invasive procedure						
No	1189	312	79.2	*Referent*		
Yes	112	28	80.0	1.05 (0.681, 1.618)	0.85 (0.44, 1.64)	–
Social factors						
No	1249	329	79.1	*Referent*		
Yes	51	11	82.3	1.22 (0.63, 2.37)	1.13 (0.41, 3.16)	–
Environmental factors						
No	1246	332	79.0	*Referent*		
Yes	54	10	84.4	1.44 (0.73, 2.86)	0.51 (0.21, 1.21)	0.64 (0.27, 1.48)
History of TB						
No	82	74	52.6	*Referent*		
Yes	1221	267	82.0	4.12 (2.93, 5.80)***	1.83 (0.93, 3.60)	2.09 (1.08, 4.06)*
Recent infection						
No	939	230	80.3	*Referent*		
Yes	335	106	76.0	0.78 (0.60, 1.01)	0.74 (0.49, 1.10)	0.74 (0.50, 1.10)
Variable	**Spinal Pain Yes**	**Spinal Pain No**	**Prevalence (%)**	**Univariable OR (95% CI) Unadjusted**	**Multivariable OR (95% CI)**	**Multivariable OR (95% CI) Final Model**
Clinical Features: Patient reported symptoms (subjective)						
Radicular pain						
No	565	318	64.0	*Referent*		
Yes	735	19	97.5	21.70 (13.5, 35.0)***	17.87 (10.31, 30.98)***	19.88 (11.66, 33.87)***
Pins and needles (LL)						
No	890	303	74.6	*Referent*		
Yes	405	37	91.6	3.73 (2.60, 5.35)***	1.35 (0.79, 2.32)	–
Numbness (LL)						
No	871	283	75.5	*Referent*		
Yes	427	58	88.0	2.39 (1.76, 3.25)***	1.04 (0.63, 1.70)	–
Weakness (LL)						
No	547	159	77.5	*Referent*		
Yes	750	181	80.6	1.20 (0.95, 1.53)	1.15 (0.77, 1.73)	–
Fatigue						
No	1092	272	80.1	*Referent*		
Yes	196	66	74.8	0.74 (0.54, 1.01)	0.48 (0.28, 1.84)**	0.50 (0.30, 0.84)**
Fever						
No	985	218	81.9	*Referent*		
Yes	311	117	72.7	0.59 (0.46, 0.76)***	0.85 (0.55, 1.32)	–
Weight loss						
No	755	216	77.8	*Referent*		
Yes	542	123	81.5	1.27 (0.98, 1.61)	1.74 (1.20, 2.52)**	1.75 (1.22, 2.50)**
Clinical Features: Clinical examination findings (objective)						
Spine tenderness						
No	771	303	71.8	*Referent*		
Yes	515	32	94.2	6.81 (4.23, 10.97)***	5.55 (3.58, 8.61)***	6.54 (4.11, 10.40)***
Dermatomes (LL)						

(*continued on next page*)

Table 3 (*continued*)

Variable	Spinal Pain		Prevalence (%)	Univariable OR (95% CI) Unadjusted	Multivariable OR (95% CI)	Multivariable OR (95% CI) Final Model
	Yes	No				
No	1081	281	79.3	*Referent*		
Yes	216	58	78.8	0.82 (0.48, 1.42)	0.89 (0.56, 1.42)	–
Myotomes (LL)						
No	903	223	80.2	*Referent*		
Yes	399	119	77.0	0.51 (0.31, 0.82)**	0.70 (0.46, 1.04)	0.51 (0.34, 0.75)***
Reflexes (LL)						
No	268	74	78.4	*Referent*		
Yes	1033	268	79.4	1.15 (0.71, 1.87)	1.05 (0.69, 1.61)	–

TB = tuberculosis. OR = Odds ratio. *** = $p < 0.001$; ** = $p < 0.01$; * = $p < 0.05$. Multivariable model included factors to determine the effect of each factor when fully adjusted. The final model included all factors in the multivariable model that met the stopping criteria of $p < 0.05$, OR >1.30 or OR < 0.77..
LL = lower-limb. OR = Odds ratio. *** = $p < 0.001$; ** = $p < 0.01$; * = $p < 0.05$. Multivariable model included factors to determine the effect of each factor when fully adjusted. The final model included all factors in the multivariable model that met the stopping criteria of $p < 0.05$, OR >1.30 or OR < 0.77.

($p < 0.05$, OR > 1.30, OR < 0.77) with spinal pain in the presence of spinal infection. In the final model, the results indicate that, for patients diagnosed with a spinal infection, the odds of those aged above 16 years presenting with spinal pain was 2.57 (95% CI: 1.36 to 4.85) to 5.33 (95% CI: 2.77 to 10.24) time greater. Further, those with a co-morbidity having spinal pain was 1.68 (95% CI: 1.09 to 2.58) times greater than those without co-morbidities. Similarly, patients with a history of TB having spinal pain were 2.09 (95% CI: 1.08 to 4.06) times greater than those without a history of TB. Weight loss was also associated with 1.75 (95% CI: 1.22 to 2.50) times greater odds. The odds of those with radicular pain or spinal tenderness having spinal pain compared to those without pain or tenderness was 19.88 (95% CI: 11.66 to 33.87) and 6.54 (95% CI: 4.11 to 10.40) greater, respectively.

Those reporting fatigue and presenting with myotomal weakness had lower odds of reporting spinal pain (OR = 0.50 95% CI: 0.30 to 0.84; OR = 0.51, 95% CI 0.34 to 0.75, respectively) than those without fatigue and myotomal weakness. A final summary of the predictors is presented in Table 4.

4. Discussion

This is the first study to examine red flags for spinal pain in patients with spinal infection using a bespoke data extraction tool based on the international framework for red flags for potential serious spinal pathologies (Finucane et al., 2020). We reviewed 124,913 case notes and found 1,645 patients, with confirmed spinal infection, a prevalence of 1.32%, from 10 centres spread across Nigeria in a 10 year period. Of those with spinal infection, 79.0% had spinal pain. We identified five factors, co-morbidity, history of TB, radicular pain, weight loss, and spine tenderness that were associated with increased odds of spinal pain whereas myotomal weakness and fatigue was associated with reduced odds of spinal pain (Table 4). In addition, age above 16 years was associated with higher prevalence of spinal pain but sex was not, with males and females having virtually identical prevalence.

Table 4
Summary of the key spinal infection risk factors associated with spinal pain.

Variable	Interpretation
Age	Patients aged above 16 years had a 2.57 to 5.33 times greater odds of spinal pain compared to those aged under 16 years.
Co-morbidity	Patients with co-morbidities have 1.68 times greater odds of spinal pain compared to those without. (e.g. Diabetes, HIV/AIDS, rheumatoid arthritis, pre-existing infections, long-term use of steroids, Cancer, Cardiovascular disease, Renal failure, Liver disease).
History of TB	Patients with a history of TB have 2.09 greater odds of reporting spinal pain compared to those without a history of TB. (Also consider those born or travelling in a TB endemic country).
Radicular Pain	Those diagnosed with a spinal infection and who experienced radicular pain were at 19.88 greater odds of spinal pain.
Weight loss	Patients who experience weight loss (3–6 months >5%) are at 1.75 greater odds of having spinal pain than those without weight loss.
Spine tenderness	Patients with spine tenderness are at 6.54 greater odds of having spinal pain than those without tenderness. (It is important to percuss the whole spine, as the area of pain reported may not be the area of infection).
Myotomal weakness	Patients presenting with myotomal weakness have reduced odds (OR = 0.50) of spinal pain. (Part of classic triad - As the nerve fails pain resolves, however, significant weakness remains).
Fatigue	Patients presenting with fatigue have reduced odds (OR = 0.51) of spinal pain.

The prevalence of spinal pain ranged from 50.9 to 100% across the 10 centres. Across the three statistical models, three centres appear to have much greater odds of spine pain in patients, whereas two centres had much lower odds (Table 3). However neither social factors nor environmental factors emerged from the analyses as being significant therefore it is difficult to explain why such variations in prevalence across centre emerged. Ohene et al. (2019) also report wide variation in the prevalence of extra-pulmonary TB across African countries and state that there is uncertainty as to the reasons for this.

Budtz et al. (2021) reported a spinal infection prevalence of 0.01% in musculoskeletal physiotherapy patients following a nationwide register-based cohort study in Denmark. In contrast we found a spinal infection prevalence of 1.32%, unsurprisingly set within the context of a Nigerian population, the vast majority of spinal infection cases were TB. The difference in the number of patients with spinal infection is not surprising and is in line with WHO country prevalence rates for TB. As stated previously Nigeria has one of the highest burdens of TB worldwide whereas Denmark has a total TB incidence of 280 with a rate of 4.9 per 100 000 per population (WHO 2020b). In a broader context it is important for musculoskeletal practitioners to note the COVID-19 pandemic has reversed years of global progress in tackling TB and TB is set to rise over the next few years as TB services are among the many disrupted by the COVID-19 pandemic. The impact on TB has been particularly severe through reduced health system capacity to provide services, less willingness and ability to seek care in the context of lockdowns, concerns about the risks of going to health care facilities during the pandemic, and stigma associated with similarities in the symptoms related to TB and COVID-19 (WHO 2021).

The literature describes a classic triad of clinical features for spinal infection; back pain, fever and neurological dysfunction (Davis et al., 2004). A previous review on spinal infection included data from 2224 patients, from 40 papers, and confirmed fever as one of the most reported clinical features (Yusuf et al., 2019), however, the current study found fever was associated with 41% lower odds of spinal pain (OR = 0.59, $p < 0.001$) and was therefore not included in our final multivariable logistic regression model. This relatively low incidence is broadly in line with the findings of Lener et al. (2018) who reported that only 50% of people with spinal infection report fever as a symptom, this is probably related to the stage of disease. One of the pathological features of spinal TB is the formation of a cold abscess which is characterized by lack of inflammation (Garg and Somvanshi 2011). The key clinical

message here is that a lack of fever cannot rule out spinal infection and clinicians should not necessarily be reassured by its absence (Finucane et al., 2020).

In terms of neurological dysfunction, we analysed separate components of neurological dysfunction and found a mixed picture. The odds of pins and needles (OR 3.73) and numbness (OR 2.39) were significantly raised but dermatomal changes (OR 0.98) and reflexes (OR 0.94) were not significantly associated with spinal pain. Interestingly myotomal weakness (OR = 0.51) was retained in the final multivariate logistic regression model as patients presenting with myotomal weakness have ($p = 0.025$) reduced odds of spinal pain. This is probably related to progression of the condition, i.e. as the nerve fails, pain resolves, however significant weakness remains. It is also important to remember that a number of risk factors for infection such as diabetes may also precipitate neurological issues.

Beyond the classic triad, radicular pain (19.88 greater odds) and spine tenderness (6.54 greater odds) emerged as risk factors in our final multivariate logistic regression model. Palpation of the spinous processes or vibration testing with a 128 Hz tuning fork is recommended to examine spinal tenderness or reproduction of symptoms further (Finucane et al., 2020). In line with Budtz et al. (2021) and Yusuf et al. (2019) older age was also generally associated with increased prevalence but in contrast to these papers, where there was an increased prevalence in men, we found men and women had very similar prevalence and odds ratios. Finucane et al. (2020) discussed patient management and described how clinicians should 'determine a level of concern' where the evidence to support red flags and the individual profile of the persons' wider health determinants e.g., age, sex, raise or lower the level of concern (index of suspicion) for the presence or absence of serious pathology. Based on our results clinicians could use the items in Table 4 to inform their level of concern for spinal infection when a patient presents with spinal pain. Any patient who raises the clinician's level of concern should then undergo a full neurological examination, and when available MRI is recommended as the imaging modality of choice when investigating suspected spinal infection (Finucane et al., 2020).

4.1. Strengths and limitations

A key strength of our study is that we specifically chose a setting where spinal infection was highly prevalent. We thus present results for a relatively large data set of 1,645 confirmed spinal infection cases for what in High or Upper Middle-Income countries is usually considered a rare condition, e.g. 0.01% (Budtz et al., 2021). Although the retrospective nature of the data collection method could be regarded as a limitation it is also a strength as it reflects a 'real world' setting. The generalisability to other countries and settings may be limited due to the very specific context, as red flags for spinal infection in High-income countries, where the burden of infectious diseases are low, would be different to those found in this study. In contrast to Nigeria where history of TB is the top red flag for spinal infection, in High-income countries, diabetes, intravenous drug use and surgery have been highlighted as important red flags associated with spinal infection (Yusuf et al., 2019). This point emphasises the need for clinicians to understand the socioeconomics and wider determinants of health present in their local populations. Due to the nature of medical records, there was insufficient data to analyse some of these wider determinants of health.

Yusuf et al. (2019) reported that spinal pain was the most common clinical feature of spinal infection but that this was only present in 72% of cases, in the current study we found 79.0% of spinal infection patients had spinal pain. The presence, or absence of specific clinical features such as spinal pain, fatigue or fever is temporally related to where patients are in the disease process. In TB there is often a prolonged prodromal stage where patients can present with vague and confusing signs and symptoms (Greenhalgh and Selfe 2010). Disease progression changes how patients will present, where early on patients are likely to have pain but those who have progressed and are actually worse will likely have less or no pain. Therefore one of the weaknesses of this paper is the focus on the presence of spinal pain.

However, clinically relevant items were extracted from the records; using a bespoke checklist based on the international framework for red flags for potential serious spinal pathologies (Finucane et al., 2020), which expert clinicians developed in response to the lack of primary evidence on serious spinal pathologies, including spinal infection.

5. Conclusion

We found a prevalence of 1.32% for spinal infection and nearly 80% of patients with confirmed spinal infection reported spinal pain. Challenges in the diagnosis of spinal infection are reported to be a result of two main issues: failure to consider spinal infection as a potential differential diagnosis and failure to recognise the relevant risk factors and clinical features (Patel et al., 2014; Khoriati et al., 2012). This paper helps raise the profile of spinal infection so it may be considered as a potential diagnosis within musculoskeletal practice. We have produced a short list of significant risk factors: Co-morbidity; Older age; Previous history of TB and clinical features: Radicular pain; Spinal tenderness; Weight loss that inform clinical decision making, these also constitute candidate variables to take into a future diagnostic accuracy study.

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References

Budtz, C., Hansen, R., Thomsen, J., Christiansen, D., 2021. The prevalence of serious pathology in musculoskeletal physiotherapy patients – a nationwide register-based cohort study. Physiotherapy 112, 96–102.

Bullock, G.S., Hughes, T., Sergeant, J.C., et al., 2021. Clinical prediction models in sports medicine: a guide for clinicians and researchers. J. Orthop. Sports Phys. Ther. 51 (10), 517–526.

Davis, D.P., Wold, R.M., Patel, R.J., et al., 2004. The clinical presentation and impact of diagnostic delays on emergency department patients with spinal epidural abscess. J. Emerg. Med. 26, 285–291.

Finucane, L., Downie, A., Mercer, C., et al., 2020. International framework for red flags for potential serious spinal pathologies. Endorsed by international federation of orthopaedic manipulative physical therapists (IFOMPT) a subgroup of the world confederation for physical therapists (WCPT). JOSPT 50, 350–372.

Garg, R.K., Somvanshi, D.S., 2011. Spinal tuberculosis: a review. The Journal of Spinal Cord Medicine 34 (5), 440–454.

GBD collaborators, G.B.D., 2017. Global, regional, and national disability-adjusted life-years (DALYs) for 333 diseases and injuries and healthy life expectancy (HALE) for 195 countries and territories, 1990–2016: a systematic analysis for the Global Burden of Disease Study 2016. Lancet 390 (10100), 1260–1344, 2017/09/16/.

Greenhalgh, S., Selfe, J., 2010. Red Flags II: A Clinical Guide to Solving Serious Spinal Pathology. Churchill Livingstone, Elsevier.

Khoriati, A., Kitson, J., Deol, R.S., 2012. Cervical spinal abscess: an insidious presentation and unusual pathology. Ann. R. Coll. Surg. Engl. 94, e184–e185.

Lener, S., Hartmann, S., Barbagallo, G.M.V., et al., 2018. Management of Spinal Infection : a Review of the Literature. American Society of Anaesthesiologists, pp. 487–496.

Ohene, S.-A., Bakker, M.I., Ojo, J., Toonstra, A., Awudi, D., Klatser, P., 2019. Extrapulmonary tuberculosis: a retrospective study of patients in Accra, Ghana. PLoS One 14 (1), e0209650. https://doi.org/10.1371/journal.pone.0209650.

Patel, A.R., Alton, T.B., Bransford, R.J., 2014. Spinal epidural abscesses: risk factors, medical versus surgical management, a retrospective review of 128 cases. Spine J. 14, 326–330.

Patel, R., Gannamani, V., Shay, E., et al., 2016. Spinal tuberculosis and cold abscess without known primary disease: case report and review of the literature. Case reports in infectious diseases 2016, 1780153. https://doi.org/10.1155/2016/1780153.

Quraishi, N.A., Hammett, T.C., Todd, D.B., et al., 2012. Malpractice litigation and the spine: the NHS perspective on 235 successful claims in England. Eur. Spine J. 21 (Suppl. 2), S196–S199.

Schirmer, P., Renault, C., Holodniy, M., 2010. Is spinal tuberculosis contagious? Int. J. Infect. Dis. 14 (8), e659–e666.

WHO, 2020a. Tuberculosis Profile: Nigeria. https://worldhealthorg.shinyapps.io/tb_profiles/?_inputs_&lan=%22EN%22&iso2=%22NG%22, 3/11/2021.

WHO, 2020b. Tuberculosis profile: Denmark. https://worldhealthorg.shinyapps.io/tb_profiles/?_inputs_&entity_type=%22country%22&lan=%22EN%22&iso2=%22DK%22, 3/11/2021.

Yusuf, M., Finucane, L., Selfe, J., 2019. Red flags for the early detection of spinal infection in back pain patients. BMC Muscoskel. Disord. 20, 606.