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A RETROSPECTIVE CROSS-SECTIONAL OBSERVATIONAL STUDY INVESTIGATING THE PREVALENT AETIOLOGIES AND CO-MORBIDITIES IN PATIENTS PRESENTING WITH VERTEBRA PLANA IN A SINGLE CENTER SPINE UNIT IN KWAZULU-NATAL, SOUTH AFRICA.

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ABSTRACT

Background
Vertebral plana (VP), characterized by the flattening of vertebrae, presents a diagnostic challenge due to its myriad causes. This study investigated the common histological diagnoses of VP within the unique healthcare context of the King Dinuzulu Hospital Complex (KDHC) Spine Unit in Durban, South Africa, to identify the most common aetiologies in this setting to guide management and prognosis.

Methods
A retrospective observational study was conducted, involving a review of medical records from January 2015 to December 2020. A cohort of 32 patients with VP was analysed for demographics, clinical presentation, imaging findings, and histological diagnoses. The primary objective was to identify prevalent histological causes, enhancing diagnostic precision.

Results
The mean age of participants was 51.1 years, with a slight female predominance. Most patients had low albumin levels and were classified as having complete neurological injury or normal neurological function. HIV status revealed a 34.4% prevalence, influencing histological diversity, while 31.25% had comorbidities, primarily hypertension. The lumbar spine, particularly L2, was frequently affected, correlating with neurologic fallout. Histological analysis revealed a surprising diversity, with multiple myeloma (26.09%) and plasmacytoma (21.74%) emerging as leading diagnoses, challenging prior assumptions. The study found no significant difference in comorbidity prevalence between genders, but a statistically significant discrepancy in the prevalence of diabetes and reduced vertebral density (RVD) between females and males.

Conclusion
This study challenges prevailing assumptions about the aetiology of VP, emphasizing the necessity for a nuanced approach to diagnostic investigations. The unexpected prevalence of multiple myeloma and plasmacytoma suggests a shift in VP aetiology, prompting a re-evaluation of clinical practices.

Recommendation
The study paves the way for further investigation into the pathophysiology and clinical features of vertebra plana. Future research should include multi-institutional diagnosis comparisons and evaluate outcomes based on early versus late or inappropriate management.

Keywords: *Vertebra plana, Spine, Atypical tuberculosis, Platyspondyly, South Africa, Multiple myeloma*
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INTRODUCTION

Vertebra plana (VP) is a radiological term that describes the collapse and flattening of a vertebral body while preserving the adjacent intervertebral disc spaces. First described by Jacques Calvé in 1925, VP is characterized by a single vertebral body exhibiting increased opacity and collapse, while the vertebral arch remains intact, and the adjacent intervertebral discs are spared. This radiological pattern is most commonly associated with

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aseptic necrosis of the vertebral body or osteochondritis [1].

The differential diagnosis of VP is broad and is often described using mnemonics such as I MELTS and FETISH. I MELTS stands for: Infection, Metastasis/Myeloma, Eosinophilic granuloma, Lymphoma/Leukaemia, and Trauma/Tuberculosis. The FETISH mnemonic represents Fracture, Eosinophilic granuloma, Tumour, Infection, Steroids (avascular necrosis), and Haemangioma [2]. Given the wide range of possible causes, a comprehensive clinical approach—incorporating a thorough history, physical examination, and appropriate laboratory and radiological investigations—is essential for accurate diagnosis. In resource-limited settings, where HIV infection is prevalent, the common causes of VP may differ from those typically described in the literature.

In such settings, tuberculosis (TB) of the spine is a frequent cause of VP, with the thoracic spine being the most commonly affected, followed by the lumbar and cervical regions. The clinical presentation of VP depends on the level of involvement, the degree of spinal cord compression, and the extent of soft tissue involvement around the spine[1].

Unlike other spinal pathologies, where a diagnosis can often be made based on typical radiological findings, VP typically requires a biopsy for a definitive diagnosis. Histological analysis is crucial not only for confirming the diagnosis but also for guiding management decisions. Patients who present with spine pathology also have neurological fallout which correlates with the level of pathology. Neurology is classified using the Frankel classification/ Asia score based on sensory, motor, and tone impairments. Tuberculosis spondylitis, a common condition in developing countries, can present with VP-like features. Tuli described a rare form of vertebra plana-like collapse in TB spondylitis, where there is central collapse of the vertebral body with the involvement of the posterior elements. Similarly, Naim-ur-Rahman et al. (1980) observed concentric collapse of the vertebral body in TB spondylitis, sparing intervertebral discs[3].

In contrast to classical VP, TB spine often presents with involvement of multiple vertebral bodies, with a predilection for endplate damage. TB spondylitis can also present as multifocal, non-contiguous vertebral involvement, necessitating full spinal imaging for accurate diagnosis.

Magnetic resonance imaging (MRI) is the preferred imaging modality for diagnosing VP due to its superior sensitivity compared to other imaging techniques. Sureka et al. described MRI findings of progressive vertebral collapse with sparing of the endplates and intervertebral discs, which may suggest a neoplastic aetiology. The convex collapse of the posterior vertebral wall is particularly characteristic of metastatic disease, with high sensitivity and specificity for identifying such lesions[3].

VP is often encountered in the context of various chronic conditions, such as lymphoma, Kümmell's disease, tuberculosis, and multiple myeloma, which can complicate the diagnostic process. Among children, eosinophilic granuloma, often associated with Langerhans cell histiocytosis, is the most common cause of VP[5].

Lymphomas, a heterogeneous group of malignancies arising from B- or T-cells, are rare as primary bone tumors but may present as VP. The incidence of lymphoma is higher in the HIV-positive population, with patients developing lymphomas at a younger age, often in their thirties. Non-Hodgkin lymphoma, in particular, has been described as a cause of VP. Spinal lymphoma typically presents with progressive back pain and nerve root or spinal cord compression symptoms that correlate with the level of involvement. Diagnosing spinal lymphoma can be challenging, as MRI findings may be non-specific, and histopathological examination may fail to provide a definitive diagnosis. Immunohistochemical studies often provide the necessary clues for accurate diagnosis, which is essential for effective treatment planning. The primary treatment for lymphoma involves chemotherapy, with radiation therapy used for local control of the disease. Surgical intervention may be required to manage symptoms related to spinal cord compression[3].

Kümmell's disease (KD) is a rare form of delayed avascular necrosis of the vertebral body following trauma. Although infrequently reported, KD can present as VP, adding to the diagnostic complexity. The typical findings in KD include intractable back pain, progressive kyphotic deformity, and delayed neurological deficits. Surgical intervention is often necessary for patients with neurological impairment, but the management of KD can be complicated by underlying factors such as poor bone quality, senile kyphosis, and local kyphotic deformity at the site of the vertebral fracture[4].

The management of VP should always be multidisciplinary, with a strong emphasis on obtaining a histological diagnosis to guide treatment. In some cases, surgical stabilization of both the anterior and posterior columns of the spine may be necessary to achieve a stable spinal construct. Recent studies suggest that kyphoplasty may offer a viable alternative to traditional corpectomy and cage insertion for restoring vertebral height, especially when combined with posterior spinal fusion[4][6].

In conclusion, diagnosing vertebra plana remains complex due to its broad differential diagnosis and overlap with other spinal pathologies. A thorough clinical evaluation, coupled with histological confirmation, is critical for directing appropriate management. While surgical approaches are often required to address the underlying pathology, emerging minimally invasive techniques, such as kyphoplasty, offer promising alternatives to conventional surgical interventions for restoring spinal stability. This study investigated the common histological diagnoses of VP

within the unique healthcare context of the King Dinuzulu Hospital Complex (KDHC) Spine Unit in Durban, South Africa, to identify the most common aetiologies in this setting to guide management and prognosis.

METHODS

Study design

A retrospective cross-sectional observational study involving the retrospective review of the medical records of patients with vertebral plana at King Dinizulu Hospital Complex (KDHC) spine unit from January 2015 to December 2020.

Study setting

The study was conducted at the King Dinuzulu Hospital Complex Spine Unit, Durban South Africa. King Dinuzulu Hospital Complex (formerly King George V Hospital) is situated in Springfield in Ward 25 of the eThekwini health district. The hospital has 400 beds of which 62 beds are reserved for the management of patients with spine pathology. The spine unit is an independent tertiary-level department that is housed at KDH. The unit caters to all the hospitals in and around Durban, the south, and north coast of KZN, and Northern inland KZN. Some cases are transferred from as far as the north-east of the Eastern Cape.

Study Sample

The study included all patients aged 18 years and above who had been diagnosed with vertebral plana at the KDHC Spine Unit during the specified period of January 2015 and December 2020. Non-probability sampling, with a preference for the purposive sampling technique, was deemed appropriate because the patients already had a working diagnosis, and the objective was to determine the cause of the diagnosis. All patients with the diagnosis of vertebrae plana during this period were reviewed. A total of 120 files were reviewed. Out of these files, only 32 fulfilled our inclusion criteria having complete files with histological diagnosis established.

Eligibility criteria

Inclusion criteria

- Medical records of all patients aged between 18-70 years.
- Medical records of patients who had a biopsy taken for vertebral plana at KDHC spine unit.

Exclusion criteria

- Patients whose biopsy results yielded inconclusive results.
- Patients who had a presumptive diagnosis but were too ill to undergo a biopsy in theatre.

Bias

To mitigate recall bias, only cases with documented histological diagnoses were included in the study, rather than relying on a patient's account of their diagnosis. The aim was to reduce selection bias by analyzing all eligible files. However, this was limited to a specific age group and this may still introduce some degree of selection bias.

Data

A data collection sheet in table format (excel) was utilized for data collection. The following variables were collected and analyzed:
Demographics (Age, Gender, and Race); Co-morbidities (HIV status, Hypertension, Diabetes Mellitus, and Malignancies); Clinical presentation (Characteristics and duration of symptoms, and Level of disease and associated neurology); Imaging studies, and Biopsy results.

Statistical analysis

Descriptive statistics such as means, medians, and standard deviations for continuous variables (e.g., age) and frequencies and percentages for categorical variables (e.g., gender, HIV status) were used to describe the demographics of the patients. Cross-tabulations and chi-squared tests were employed to explore associations between demographics (e.g., age, gender) and co-morbidities (e.g., HIV status). Descriptive statistics were again used to summarize continuous variables related to clinical presentation, such as the duration of symptoms. For categorical variables related to clinical presentation, such as the presence of specific symptoms, frequencies, and percentages were calculated. Descriptive statistics were also used to summarize which vertebrae are most affected by VP. Descriptive statistics were again used to summarize histological findings, providing frequencies and percentages for various diagnoses. Frequencies and percentages were used to describe the types of treatment received by patients diagnosed with VP. All statistical procedures were performed on IBM SPSS version 26 running under Microsoft Windows for a personal computer. Statistical significance testing was two-sided at a significance level of 0,05 (5%).

Ethics

This study was approved by the Biomedical Research Ethics Committee at the University of KwaZulu Natal, South Africa (BREC/00004908/2022) and received approval from the Department of Health (KZ_202211_027) on 24 February 2023.

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RESULTS

Demographics (Age and Gender)

The medical records of 32 patients were reviewed and analyzed. The mean age of all participants was 51.1 (±13.1) years. The youngest among the participants was 18 years and the oldest was 73 years old. There were 17 (53.1%) females and 15 (46.9%) male participants. The mean of females was 54.29 (±11.9308) years as compared to 47.53 (±13.8350) years for males. Females were slightly older (6.76 years); however, the difference was not statistically significant (p-value 0.0740).

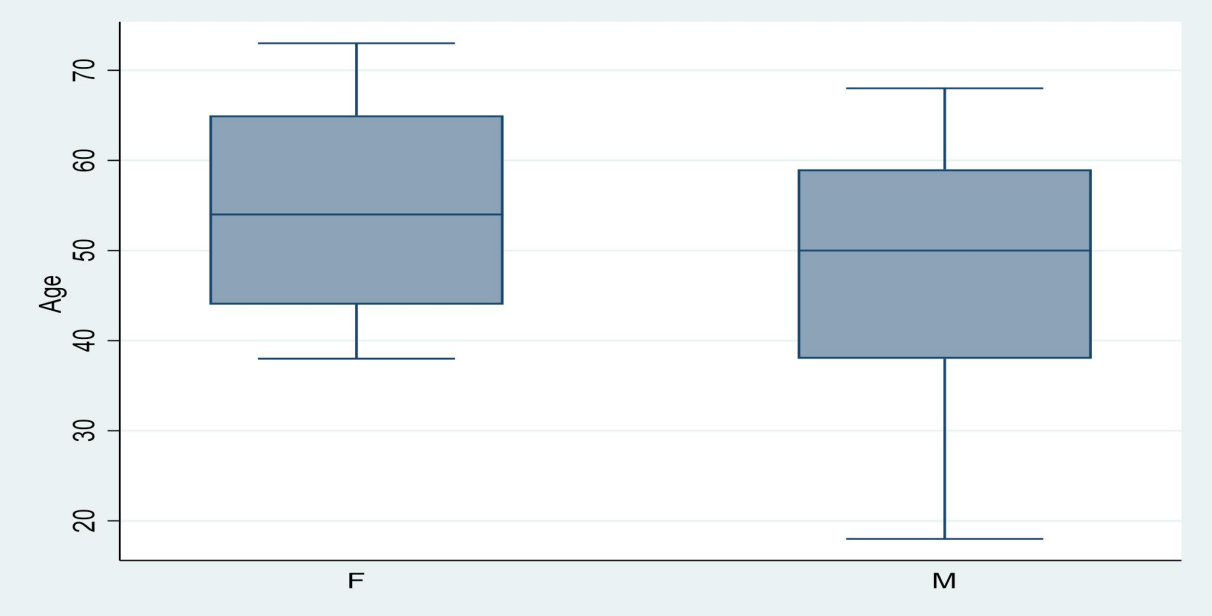

Figure 1: Comparison of mean ages of Female vs. male patients presenting with VP

HIV status and comorbidities

A total of 11 patients (34.4%) were reported to be HIV positive. Only 10 patients (31.25%) had comorbidities. All 10 patients with comorbidities were hypertensive, however, only 4 (12.50%) were diabetic.

Table 1: HIV status and comorbidities of participants

Clinical Characteristics	Frequency	Percentage
RVD		
Positive	*11*	*34.4%*
Negative	*21*	*65.6%*
Comorbidities	10	31.25%
Diabetes Mellitus	*4*	*12.50%*
Hypertension	*10*	*31.25%*

Albumin Levels of Patients

Most patients (n=19; 61.29%) had a low albumin level, followed by normal (n=11; 35.48%), while only 1 patient (3.23%) had a high albumin level (Figure 2). The mean albumin was 32 (±7.0).

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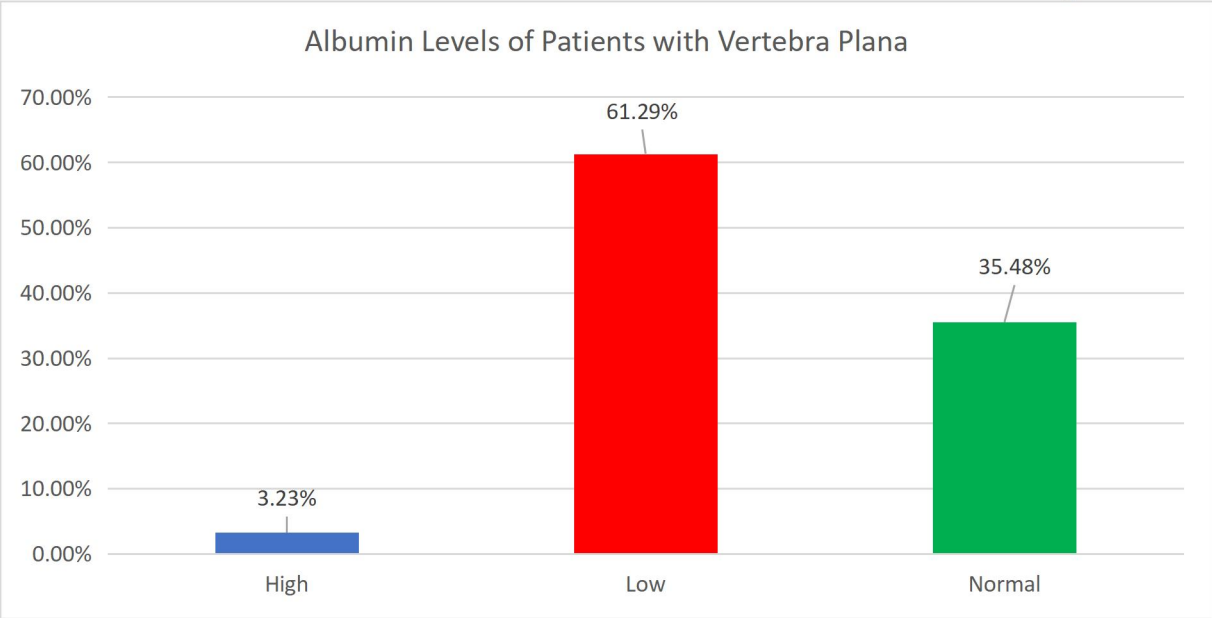

Figure 2: Albumin Levels of Patients with Vertebra Plana

Frankel class of patients with Vertebra plana

The distribution of patients in this study revealed that the largest proportion fell into both Class A (Complete Neurological Injury) and Class E (Normal Neurological Function), each accounting for 34.38% of the total. Following closely were individuals classified as Class D (Motor Incomplete, Functional) at 18.75%, while Class C (Motor Incomplete, Non-Functional) constituted 9.38% of the cohort. The smallest representation was observed in Class B (Sensory Incomplete), comprising just 3.13% of the patient population.

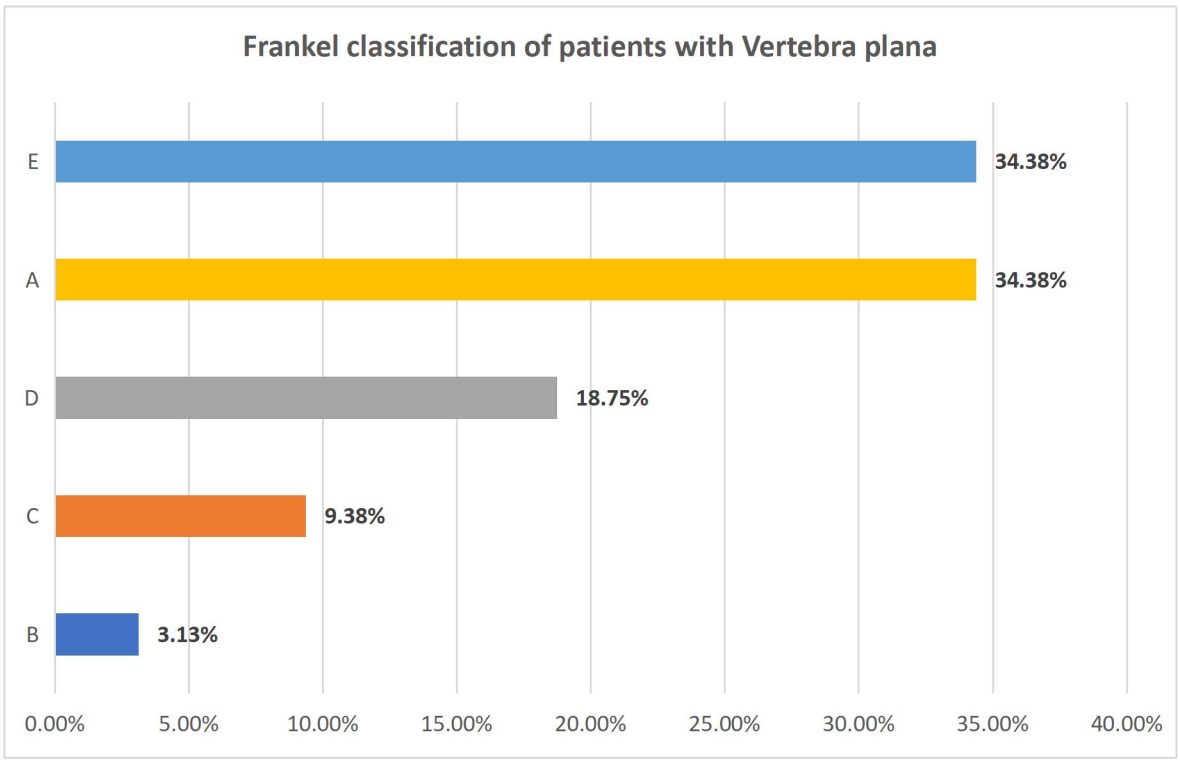

Figure 3: Frankel class of patients with Vertebra plana

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The level of vertebra affected

Figure 4 depicts that L2 was the most impacted vertebra (16.13%), with T6 following closely behind (12.90%), while C3 exhibited the least impact (3.23%). This suggests that L2 is the commonly affected vertebra in the presence of any associated lesions in and around the spine.

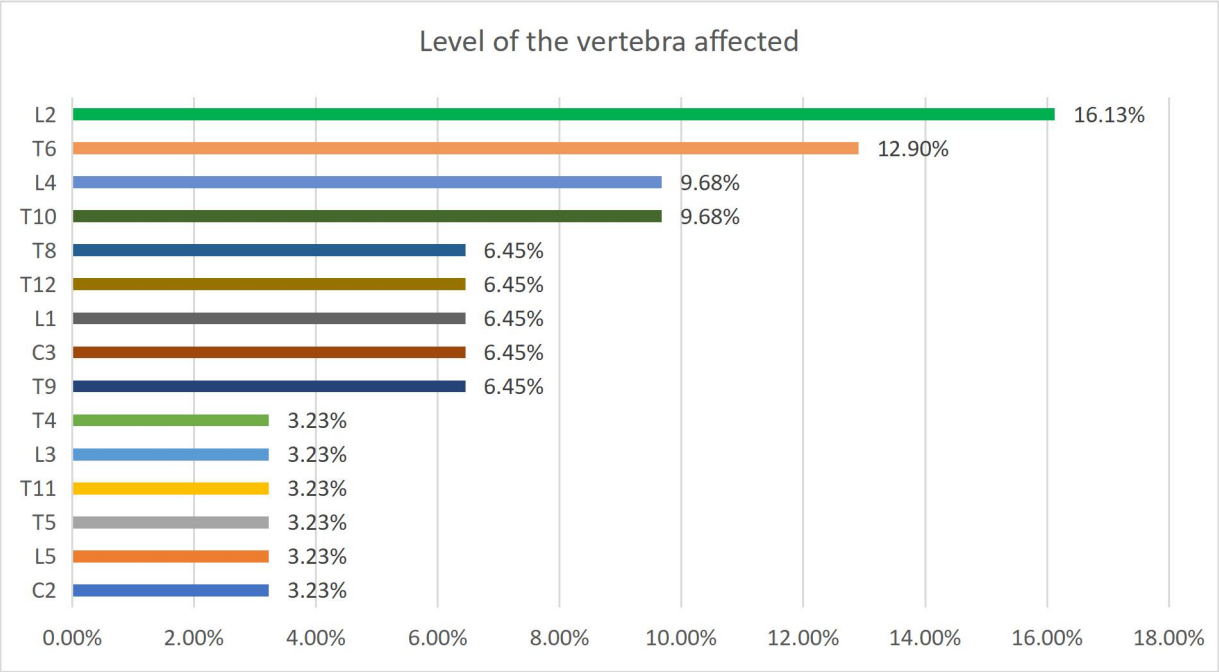

Figure 4: Level of vertebra affected

Histological examination findings

Histological examination findings in the study reveal that the predominant histological type was MM (26.09%), followed by plasmacytoma (21.74%), TB (17.39%), and NHL (13.04%). The least prevalent histological type recorded was breast cancer (4.35%), as illustrated in Figure 5.

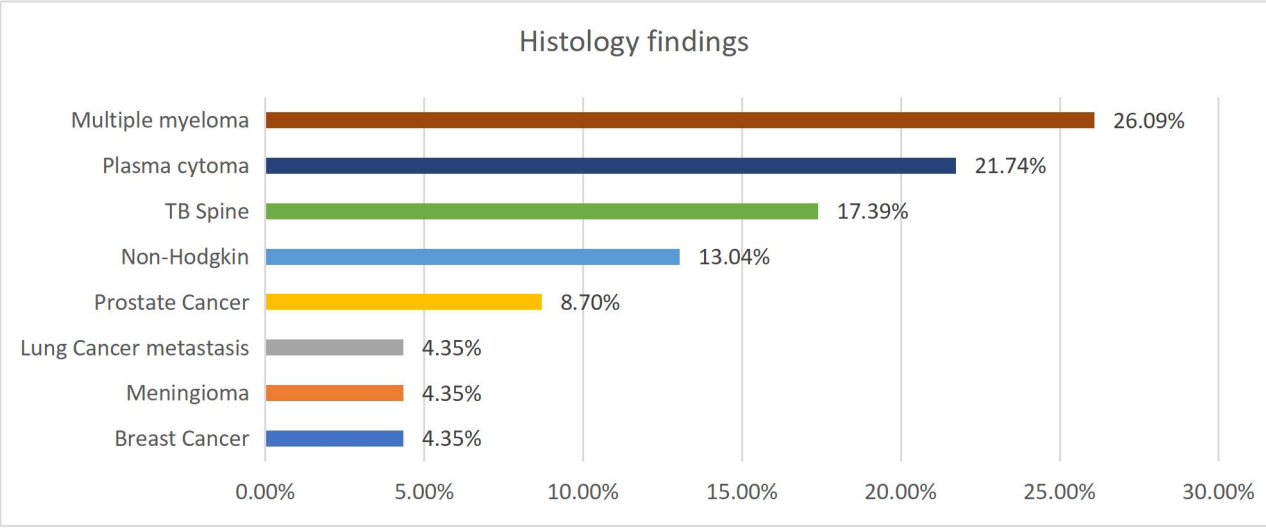

Figure 5: Histological examination findings

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Association between clinical characteristics and gender

Table 2 illustrates that among the patients included in the study, 70.00% of females had comorbidities, compared to 30.00% of males. The statistical analysis indicated that there was no statistically significant difference in the prevalence of comorbidities between genders (p-value = 0.197). Out of the 4 patients diagnosed with diabetes, all were females (100.0%), while none of the males (0.0%) had diabetes. This discrepancy demonstrated a statistically significant difference in the prevalence of diabetes between females and males (p-value = 0.045). When assessing the presence of hypertension about gender, the findings suggested that there was no statistically significant difference in the prevalence of hypertension between genders (p-value = 0.197). Regarding the prevalence of HIV, the results indicated a statistically significant difference in its prevalence between females and males (p-value = 0.034). For albumin levels categorized as "High," "Normal," and "Low," the analysis revealed that the differences in albumin levels between females and males were not statistically significant (p-value = 0.450).

Table 2: Association between clinical characteristics and gender

	Female	Male	P value
Comorbidities	7 (70.00%)	3 (30.00%)	0.197
Diabetes	4 (100.0%)	0 (0.00%)	0.045
Hypertension	7 (70.00%)	3 (30.00%)	0.197
RVD	3 (27.27%)	8 (72.73%)	0.034
Albumin level			
High	0 (0.0%)	1 (100.0%)	
Normal	7 (63.64%)	4 (36.36%)	0.450
Low	10 (52.63%)	9 (47.37%)	

DISCUSSION

Vertebra plana was initially believed to originate from aseptic necrosis of the vertebral body or osteochondritis. The features of a 'true' vertebra plana include: the involvement of a single vertebra, preserved adjacent intervertebral disc, widening of the intervertebral disc, and sclerosis or greater opacification of the involved vertebral body. (1) The differential diagnosis is quite vast, especially in developing countries where the burden of infectious disease is still a great challenge. This makes it vital that a detailed history, physical examination, and investigations including radiological, and radiology-assisted biopsy are documented to facilitate prompt and directed management of patients.

The study results reported that the age of patients affected by the disease was below the age of 60 years (with the majority of patients falling between 47- 54 years). The majority of patients were female accounting for 53.1%. The total number of patients with HIV infection was 34.4% with the majority being male. The Frankel classification directly correlated with the level of pathology, L2 was the most common level (Frankel D), the higher the level the higher the neurological fallout, as demonstrated in the results section, with most cases falling at Frankel A between C2 and L1. The cases that had advanced neurology correlated with the level of pathology as expected for the level. Histology which came up with a diagnosis of NHL had less neurological fallout for the level affected as described in literature. In the setting, all these patients were noted to be HIV positive.

Most of the patients included in the study demonstrated low albumin levels (61.1%) which is of significance as albumin is one of the parameters used to assess the general nutrition of the patient and clinical wellness of the patient. 26% of histological samples yielded a diagnosis of multiple myeloma, 21,74& showed plasmacytoma, 17,39% revealed a diagnosis of TB, and 13, 04% was consistent with NHL. The incidence of other tumors (metastasis from either prostate, breast, and lung, benign primary bone tumors-osteoblastoma) accounted for a minority as seen in Figure 4. The main reason for the discrepancy in the findings was the fact that the study excluded the pediatric population, which is the population that comes up in the literature for vertebra plana. (5)

Interpretation

The findings of this study challenged our initial assumption that tuberculosis (TB) was the predominant etiology of vertebra plana (VP). Our results revealed that multiple myeloma (MM) was the leading diagnosis, accounting for 26.09% of cases, while TB was responsible for only 17.39% of cases. Although the gender distribution in our study showed a higher proportion of females than males, this difference was not statistically significant.

Biochemical analysis indicated a high prevalence of malnutrition within the sample population, with 61.2% exhibiting low albumin levels. HIV was identified as a significant comorbidity, affecting 34.4% of participants, while diabetes and hypertension were less common, with prevalences of 12.5% and 1.25%, respectively.
Neurological outcomes were evenly distributed between Frankel grades A and E, each representing 34.8% of cases. These outcomes were closely associated with the

level of spinal involvement, as demonstrated in the accompanying tables.

GENERALIZABILITY

This study was conducted at a single center with a relatively small sample size. The rarity of the condition, combined with the limited availability of biopsy samples, restricted our ability to expand the cohort, even though the study spanned an extended period. To strengthen the generalizability of our findings, a larger sample size is required, both within our local population and in broader international contexts.

CONCLUSIONS

Vertebra plana represents a rare manifestation of spinal pathology, accounting for approximately 2% of all spinal lesions. This study identifies the most common histological diagnoses of vertebra plana at the King Dinuzulu Hospital Complex Spine Unit as multiple myeloma, plasmacytoma, tuberculosis, and non-Hodgkin lymphoma. The findings underscore the importance of comprehensive investigation and individualized management for patients presenting with atypical spinal lesions, particularly in the context of HIV in developing countries, where not all cases are infectious. It is crucial to recognize that atypical spinal lesions are not invariably indicative of infection. A thorough patient evaluation, including detailed history taking, clinical examination, and a combination of hematological, radiological, and histological investigations, is essential for accurate diagnosis and early intervention.

Furthermore, the study emphasizes a key takeaway for the developing world: not all HIV-positive individuals with spinal lesions present with tuberculosis. The study suggests that future research should focus on a comparative analysis of diagnoses across multiple institutions, including pediatric populations, to better understand variations in management practices and the outcomes of early versus late or inappropriate management.

The research also revealed a broader range of aetiologies for vertebra plana than traditionally reported, with multiple myeloma and plasmacytoma emerging as the leading causes. This finding contrasts with earlier studies, which often cited Langerhans cell histiocytosis, osteoporosis, and other metabolic disorders as common aetiologies. The results emphasize the need for a holistic, individualized approach to the diagnosis and management of atypical spinal lesions, with particular attention to the importance of comprehensive diagnostic workup to ensure appropriate treatment.

LIMITATIONS

Due to the rarity of vertebra plana, the small sample size may limit the generalizability of the findings. Additionally, the study was conducted at an institution with outdated, non-digital record-keeping systems, which posed challenges in tracking patient records and resulted in missing data in some cases. As a result, certain cases were excluded from the analysis due to incomplete information. Another limitation was the scarcity of comprehensive literature on vertebra plana, as most prior reports are individual case studies with limited data.

RECOMMENDATIONS

The study underscores the critical importance of performing a routine biopsy in patients presenting with a clinical diagnosis of vertebra plana, as the aetiology of this condition can vary significantly and may differ from initial presumptions.

Historically, tuberculosis (TB) was considered the primary cause of vertebra plana (VP), particularly in developing countries where infectious diseases are prevalent due to factors such as poverty, malnutrition, and a high incidence of HIV infection. This assumption often led to prolonged, empiric TB treatment, which in many cases resulted in little to no clinical improvement. Patients were subsequently referred for further investigation at higher-tier institutions only after failing to respond to TB therapy.

This study highlights the need for a more nuanced approach to the diagnosis of VP, emphasizing the importance of ruling out alternative aetiologies. It opens the door for future research into the pathophysiology of VP and the clinical variability observed across different patient populations. Future studies should include multi-institutional diagnostic comparisons, with a particular focus on the pediatric population, and should assess patient outcomes based on the timing and appropriateness of management, especially in cases of early versus delayed or misdiagnosed treatment.

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AUTHOR CONTRIBUTION

Dr Zovuyo Mgoduka was responsible for putting the study together data collection and initial write-up. Dr. Malleck Gunseli was responsible for editing the write-up and editing the final write-up for submission.
Dr Alberto Puddu and Dr Sepeleng Mabusha who work in the spine unit assisted in putting together the study objectives, inclusion, and exclusion criteria.

DATA AVAILABILITY

Data is available with the primary author of the if is requested. Currently stored in a locked file in the author's computer.

LIST OF ABBREVIATIONS

MM- Multiple myeloma
NHL- Non-Hodgkin's lymphoma
RVD- Retroviral disease
HIV- Human immunodeficiency virus
BC- Bone carcinoma
CA- Carcinoma
TB- Tuberculosis
HPT- Hypertension
DM- Diabetes
VP- Vertebra Plana

CONFLICT OF INTEREST

No conflicts to report.

FUNDING

The study was not funded.

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