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Original Research Article

EFFECT OF INTRAVENOUS ZOLEDRONIC ACID ON PAIN, FUNCTION AND BONE MINERAL DENSITY IN PATIENTS WITH VERTEBRAL OSTEOPOROSIS PRESENTING WITH BACK PAIN

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ABSTRACT

Background: Vertebral osteoporosis is a frequent, often overlooked cause of chronic back pain. Zoledronic acid is an effective once-yearly bisphosphonate, but its effect on pain and function in back-pain patients with vertebral osteoporosis is not well described. **Materials and Methods:** In this prospective study at a tertiary hospital in South India, adults ≥40 years with back pain >4 weeks were screened by DXA. Of 120 patients, 50 (41.7%) with lumbar spine osteoporosis received a single 5 mg intravenous zoledronic acid infusion plus calcium and vitamin D. Back pain (Visual Analogue Scale, VAS) and disability (Modified Oswestry questionnaire) were recorded at baseline, 12 and 24 weeks, and 1 year. AP lumbar spine BMD was measured by DXA at baseline and 1 year. Within-patient changes were analysed using paired t-tests. **Result:** Mean lumbar BMD remained essentially stable over 1 year. Mean VAS scores fell by about 1 point at 12 and 24 weeks ($P < 0.001$), with a smaller but still significant improvement at 1 year ($P = 0.019$). Oswestry scores improved modestly at 12 and 24 weeks but were not significantly different from baseline at 1 year. **Conclusion:** In adults with back pain and DXA-confirmed vertebral osteoporosis, zoledronic acid stabilised lumbar BMD and produced short to medium-term pain relief, while functional gains were limited and not sustained. The high osteoporosis yield among back-pain patients supports routine osteoporosis screening and multimodal management in this population.

INTRODUCTION

Osteoporosis is a systemic skeletal disorder characterized by low bone mass and microarchitectural deterioration of bone tissue, leading to increased fragility and risk of fracture. Vertebral fractures are among the most common and earliest clinical manifestations of osteoporosis and are a major cause of chronic back pain, height loss, kyphosis and disability in older adults. The global burden of osteoporosis is substantial, with meta-analyses suggesting that roughly one in four older adults are affected, and data from India indicate a particularly high prevalence, with estimates of osteoporosis in Indian adults ranging from about 20–35% depending on age, sex and skeletal site.[1] Projections further suggest that by 2050 more than half of osteoporotic fractures worldwide will occur in Asia, underlining the urgency for early detection and effective treatment strategies in this region.[2]

Vertebral osteoporosis is often clinically silent until a fragility fracture occurs; however, many patients first present to outpatient clinics with persistent or recurrent back pain, which may be the only clue to underlying bone fragility. Epidemiological data show that vertebral osteopenia and osteoporosis are highly prevalent in individuals over 50 years of age, particularly women, and vertebral fractures may be present in up to 15–20% of older adults in some cohorts.[3,4] In India, community-based studies have reported osteoporosis in 15–25% of men and women in the 40–75-year age group, with even higher rates in postmenopausal women, yet many of these individuals remain undiagnosed until they present with pain or low-energy fractures. Back pain is one of the most frequent musculoskeletal complaints in middle-aged and older adults, but the proportion of these patients who have underlying vertebral osteoporosis is not routinely assessed in many clinical settings. Understanding the incidence of osteoporosis among patients presenting with back

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pain above 40 years of age is therefore important for designing targeted screening and intervention strategies.[5,6]

Management of vertebral osteoporosis and associated back pain typically combines non-pharmacological measures, adequate calcium and vitamin D supplementation, and anti-osteoporotic pharmacotherapy. Among the available drugs, nitrogen-containing bisphosphonates remain a cornerstone of treatment.[7] These agents bind avidly to hydroxyapatite in bone and are taken up by osteoclasts during bone resorption; within osteoclasts they inhibit farnesyl pyrophosphate synthase in the mevalonate pathway, leading to impaired prenylation of small GTPase proteins, disruption of osteoclast function and induction of apoptosis. This mechanism results in marked suppression of bone turnover and progressive gains in bone mineral density (BMD), with corresponding reductions in fracture risk.

Zoledronic acid is a third-generation, highly potent, nitrogen-containing bisphosphonate that is administered as a short intravenous infusion, most commonly at a dose of 5 mg once yearly for the treatment of osteoporosis. Large randomized controlled trials such as the HORIZON-Pivotal Fracture Trial have demonstrated that annual zoledronic acid infusions significantly increase BMD and reduce the risk of vertebral, hip and other fractures in postmenopausal women with osteoporosis. Subsequent analyses have also shown that zoledronic acid therapy can reduce the number of days with back pain and activity limitation due to vertebral fractures, suggesting a potential benefit not only on structural bone outcomes but also on patient-reported pain and functional status. Real-world and extension studies further support the durability of these effects over several years of treatment.[8, 9]

Despite this robust evidence base for fracture prevention, there are relatively fewer data focusing specifically on the short- to medium-term impact of intravenous zoledronic acid on back pain intensity and functional disability in patients who present primarily with back pain and are then found to have vertebral osteoporosis. Most pivotal trials enrolled patients on the basis of BMD or prevalent vertebral fractures rather than symptomatic back pain as the primary complaint, and they often reported back pain as a secondary outcome.[10,11] Moreover, there is limited information from Indian and other resource-limited settings on the incidence of osteoporosis among patients over 40 years of age presenting with back pain to orthopedic or spine clinics, where opportunities for early diagnosis using bone mineral density assessment (e.g., dual-energy X-ray absorptiometry) could be maximized.

In this context, evaluating the role of zoledronic acid in a pragmatic cohort of patients with back pain associated with vertebral osteoporosis is clinically relevant. An intervention that can simultaneously improve pain, enhance functional capacity, and increase BMD with a convenient once-yearly infusion may have substantial advantages in terms of adherence, quality of life and long-term fracture prevention, especially in busy public-sector or semi-urban practices. At the same time, quantifying how frequently osteoporosis is encountered among patients over 40 years presenting with back pain can highlight the need for routine bone health evaluation in this group.

Therefore, the present study was undertaken to determine the effect of intravenous zoledronic acid in patients presenting with back pain associated with vertebral osteoporosis, specifically in terms of pain relief, functional improvement and changes in bone mineral density, and to estimate the incidence of osteoporosis in patients above 40 years of age presenting with back pain.

Aims and Objectives

The present study is designed to evaluate the clinical and densitometric effects of intravenous zoledronic acid in patients with back pain associated with vertebral osteoporosis, and to explore the burden of underlying osteoporosis among adults presenting with back pain.

MATERIALS AND METHODS

Study Setting and Period

The study was conducted at Government Medical College is a medical institute located in Anantapuramu, Andhra Pradesh, India. Patients were recruited over a period of 22 months, from October 2022 to august 2024.

Study Population

Patients of either sex, aged 40 years and above, presenting with back pain of more than 4 weeks' duration to the outpatient departments of the study hospitals were screened for eligibility. A total of 120 patients with back pain were initially evaluated. Those who were found to have osteoporosis on bone mineral density (BMD) assessment were considered for inclusion in the study. Written informed consent was obtained from all participants prior to enrolment.

Inclusion Criteria

Patients were eligible for inclusion if they were aged 40 years or older (either sex), provided written informed consent, and had back pain of more than 4 weeks' duration that was not adequately relieved by usual medications and exercises. In cases where magnetic resonance imaging (MRI) had been performed, only those patients whose MRI did not show degenerative disc changes were considered for the study.

Exclusion Criteria

Patients were excluded if they were younger than 40 years; had primary or secondary bone tumours; were already receiving treatment for osteoporosis for more than 3 months; presented more than 3 months after sustaining a fracture; had undergone surgery for a fracture more than 3 months prior to presentation; or had associated metabolic or systemic diseases such as diabetes mellitus, hypertension, hyperthyroidism or hyperparathyroidism.

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Clinical Evaluation and Baseline Investigations

All patients underwent detailed demographic profiling and thorough clinical examination, followed by a standardized panel of baseline investigations including complete blood count, bleeding time and clotting time, random blood sugar, serum creatinine and blood urea, electrocardiogram, serum calcium and phosphate, and plain radiographs of the dorsolumbar and lumbosacral spine. Additional assessments, such as extended routine blood tests, serum alkaline phosphatase, abdominal ultrasonography, dual-energy X-ray absorptiometry (DXA) and magnetic resonance imaging (MRI) of the spine were performed in selected cases as clinically indicated.

Bone Mineral Density Assessment

BMD was measured using a GE Healthcare Lunar Prodigy encore-based dual-energy X-ray absorptiometry (DXA) bone densitometer. Measurements were obtained from the anteroposterior (AP) lumbar spine. Morphometric analysis of vertebral bodies was performed using lateral vertebral assessment.

The diagnosis of osteoporosis was established according to the National Osteoporosis Foundation (NOF) 2013 guidelines. Patients identified as osteoporotic on DXA formed the study group for intervention with zoledronic acid.

Intervention Protocol

Patients diagnosed with osteoporosis were counselled regarding the nature of the disease and the treatment protocol. Adequate oral hydration was advised prior to intravenous therapy.

Each patient received a single dose of 5 mg zoledronic acid administered intravenously over a minimum period of 15 minutes after confirming eligibility and obtaining informed consent for the infusion. Patients were observed for at least 24 hours following infusion for any allergic or acute adverse reactions. Prophylactic antipyretic medication with paracetamol was prescribed to minimize acute-phase reactions.

All patients were advised to continue calcium and vitamin D supplementation throughout the study period. For post-infusion pain management, only topical analgesic applications were permitted; systemic analgesics were avoided to prevent confounding of pain assessment.

Outcome Measures and Follow-up

Clinical outcomes were evaluated in terms of pain and functional status. Back pain intensity was measured using the Visual Analogue Scale (VAS), and functional disability was assessed with the Modified Oswestry Back Pain Disability Questionnaire. Patients were examined at baseline and then reassessed at 12 weeks, 24 weeks and 1 year after the zoledronic acid infusion using these instruments. In addition, AP lumbar spine BMD was re-evaluated by DXA at 1 year to quantify changes in bone mineral density relative to baseline.

Data Handling

All clinical, radiological, densitometric and questionnaire-based data were recorded in a structured study proforma. The collected data were compiled and interpreted to determine the effect of intravenous zoledronic acid on pain, function and BMD, and to estimate the incidence of osteoporosis among patients over 40 years presenting with back pain.

Follow-up Schedule and Outcome Assessment

All eligible patients who received zoledronic acid were followed prospectively at four predefined time points over 1 year. At Visit 1 (Day 1, baseline), patients were screened against the inclusion and exclusion criteria, written informed consent was obtained, and detailed demographic data, medical history, concomitant medications and a thorough physical examination were recorded. Baseline investigations included complete blood picture, renal function tests (serum urea and creatinine), serum calcium, phosphate and alkaline phosphatase, lumbar spine radiographs and DXA-based lumbar spine BMD assessment. In patients with features suggestive of radiculopathy, an MRI of the lumbosacral spine and/or neurosurgical opinion was obtained. Those confirmed to have osteoporosis on DXA and deemed eligible received a single 5 mg intravenous infusion of zoledronic acid, after which they were observed for approximately 24 hours for acute adverse reactions, either as outpatients or inpatients as clinically indicated.

At Visit 2 (Week 12), back pain and functional disability were reassessed using the Visual Analogue Scale (VAS) and the Modified Oswestry back pain questionnaire, and all observed or spontaneously reported adverse events since the previous visit were documented. Vital signs, including pulse rate and blood pressure, were also recorded.

At Visit 3 (Week 24), VAS and Modified Oswestry scores were again recorded to evaluate changes in pain and function, any new or ongoing adverse events were documented, and pulse rate and blood pressure were measured.

At Visit 4 (1 year), final assessment of pain and functional status was performed using the VAS and Modified Oswestry questionnaire, all adverse events occurring during the entire study period were reviewed, and vital signs were recorded. Lumbar spine BMD was reassessed by DXA to quantify changes relative to baseline. Completion of the 1-year evaluation marked the end of follow-up for each patient.

Statistical Analysis

Descriptive and inferential statistics were used for data analysis. Continuous variables were presented as mean ± standard deviation (SD) with minimum and maximum values, and categorical variables as frequencies and percentages. A two-sided P value < 0.05 was considered statistically significant. The analysis assumed that (i) the dependent variables were approximately normally distributed, (ii) the sample was representative of the target population

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and (iii) observations were independent. Within-group changes in continuous outcomes (VAS scores, Oswestry scores and BMD) between baseline and follow-up visits were assessed using the paired, two-tailed Student's t-test. For interpreting P values, $0.05 < P < 0.10$ was regarded as suggestive, $0.01 < P \leq 0.05$ as moderately significant and $P \leq 0.01$ as strongly significant. All analyses were performed using SPSS and OriginPro.

RESULTS

During the study period, 120 patients aged 40 years or older with back pains of more than 4 weeks' duration were screened. Of these, 50 patients (41.7%) were diagnosed with osteoporosis on DXA and were enrolled into the study, whereas 70 patients (58.3%) were non-osteoporotic or did not meet the inclusion criteria and were excluded from the intervention phase.

Demographic Profile

A total of 120 patients aged above 40 years presenting with back pain were screened during the study period. Of these, 50 patients (those confirmed to be osteoporotic on DXA) met the eligibility criteria and were included in the final analysis.

Age Distribution

Among the 50 osteoporotic patients, the largest proportion belonged to the 51–60 years age group (n = 20, 40%), followed by the 41–50 years group (n = 17, 34%) and the 61–70 years group (n = 11, 22%). Only a small proportion of patients were aged 71–80 years (n = 2, 4%), indicating that the majority of osteoporotic individuals with back pain were in the fifth and sixth decades of life.

Gender Distribution

There was a clear female preponderance among the study population. Of the 50 osteoporotic patients included, 30 were females (60%) and 20 were males (40%), indicating that women constituted the majority of patients with vertebral osteoporosis presenting with back pain (Figure 2)

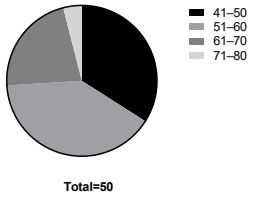

Figure 1

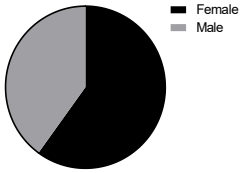

Figure 2

Figure 1: Age-wise distribution of osteoporotic patients included in the study; Figure 2: Gender-wise distribution of osteoporotic patients included in the study.

Gender-Specific Age Distribution

Gender-specific age distribution showed that both females and males were predominantly clustered in the 51–60-year age group (Table 1). Among females, 33.3% were in the 41–50-year group and another 33.3% in the 51–60-year group, while 26.7% and 6.7% were in the 61–70 and 71–80-year groups, respectively. In males, half of the patients (50.0%) were in the 51–60-year group, followed by 35.0% in the 41–50-year group and 15.0% in the 61–70-year group, with no male patients above 70 years. Overall, 40.0% of the study population belonged to the 51–60-year group, reinforcing that the fifth and sixth decades formed the peak age for vertebral osteoporosis presenting with back pain.

Table 1: Gender-specific age distribution of patients studied

Age in years	Female (n=30)	Male (n=20)	Total (n=50)
41–50	10 (33.3%)	7 (35.0%)	17 (34.0%)
51–60	10 (33.3%)	10 (50.0%)	20 (40.0%)
61–70	8 (26.7%)	3 (15.0%)	11 (22.0%)
71–80	2 (6.7%)	0 (0.0%)	2 (4.0%)

Bone Mineral Density (DXA – AP Lumbar Spine)

The mean AP lumbar spine BMD at baseline was 0.7526, and at the 1-year follow-up it was 0.7542, indicating only a minimal net change over the study period. The distribution of patients across BMD categories at baseline and at 1 year is shown in Table 2.

Overall, the majority of patients remained within the 0.71–0.80 BMD range at both time points, with a slight shift from the lowest BMD category (≤0.70) towards the 0.71–0.80 and 0.91–1.0 ranges, suggesting stabilization of bone density rather than marked deterioration.

Table 2: DXA AP spine (average BMD) at baseline and 1 year (n = 50)

DXA AP spine (Avg BMD)	Initial scan n (%)	At 1 year n (%)	% change*
≤ 0.70	16 (32.0%)	15 (30.0%)	−2.0%
0.71–0.80	25 (50.0%)	27 (54.0%)	+4.0%
0.81–0.90	9 (18.0%)	7 (14.0%)	−4.0%
0.91–1.00	0 (0.0%)	1 (2.0%)	+2.0%

*% change indicates the absolute change in the proportion of patients in each BMD category over 1 year.

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Overall, BMD remained essentially stable, with mild redistribution towards the 0.71–0.80 and 0.91–1.0 BMD categories over the 1-year follow-up.

Lateral Vertebral Assessment – Thoracic Spine

Lateral vertebral assessment of the thoracic spine demonstrated that most levels were structurally preserved (Table 3). Vertebrae T5, T8, T9 and T10 were normal in all patients. At T4, mild deformity was observed in 4.0% of patients. The highest concentration of abnormalities occurred at T6, where 8.0% of vertebrae were deformed (2.0% mild, 4.0% moderate and 2.0% severe). Moderate deformities were also seen at T7 in 4.0% of patients. In the lower thoracic region, T11 and T12 showed abnormalities in 10.0% of patients each, predominantly of mild to moderate grade. Severe deformity was confined to T6.

Table 3: Lateral vertebral assessment (LVA) – thoracic spine

Vertebra	Normal n (%)	Mild n (%)	Moderate n (%)	Severe n (%)
T4	48 (96.0%)	2 (4.0%)	0 (0.0%)	0 (0.0%)
T5	50 (100.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
T6	46 (92.0%)	1 (2.0%)	2 (4.0%)	1 (2.0%)
T7	48 (96.0%)	0 (0.0%)	2 (4.0%)	0 (0.0%)
T8	50 (100.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
T9	50 (100.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
T10	50 (100.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
T11	45 (90.0%)	3 (6.0%)	2 (4.0%)	0 (0.0%)
T12	45 (90.0%)	2 (4.0%)	3 (6.0%)	0 (0.0%)

Lateral Vertebral Assessment – Lumbar Spine

In contrast to the thoracic region, vertebral deformities were more frequent in the lumbar spine (Table 4). L1 was the most commonly affected level, with 32.0% of vertebrae showing deformity (14.0% mild, 16.0% moderate and 2.0% severe). At L2, abnormalities were seen in 18.0% of patients (8.0% mild, 6.0% moderate and 4.0% severe). L3 showed 16.0% deformity (8.0% mild and 8.0% moderate) without severe changes, while L4 demonstrated deformity in 24.0% of patients (14.0% mild and 10.0% moderate). Overall, deformities in the lumbar spine were predominantly mild to moderate, with severe compression fractures being relatively uncommon.

Table 4: Lateral vertebral assessment (LVA) – lumbar spine

Vertebra	Normal n (%)	Mild n (%)	Moderate n (%)	Severe n (%)
L1	34 (68.0%)	7 (14.0%)	8 (16.0%)	1 (2.0%)
L2	41 (82.0%)	4 (8.0%)	3 (6.0%)	2 (4.0%)
L3	42 (84.0%)	4 (8.0%)	4 (8.0%)	0 (0.0%)
L4	38 (76.0%)	7 (14.0%)	5 (10.0%)	0 (0.0%)

Pain Assessment – Visual Analogue Scale (VAS)

At baseline, patients reported high pain intensity; with a mean VAS score of 7.46 ± 0.91 (range 6.00–9.30). Following zoledronic acid infusion, there was a statistically significant reduction in pain at both 12 and 24 weeks. Mean VAS scores decreased to 6.41 ± 0.74 at 12 weeks (mean reduction vs baseline 1.052; $t = 7.237$; $P < 0.001$) and 6.44 ± 0.64 at 24 weeks (mean reduction 1.028; $t = 10.271$; $P < 0.001$), indicating a clinically meaningful improvement in back pain (Table-5).

By 1 year, some attenuation of this effect was observed; with the mean VAS score rising to 7.16 ± 0.73 (range 5.80–9.00). However, pain intensity remained modestly but significantly lower than at baseline (mean difference 0.300; $t = 2.420$; $P = 0.019$), suggesting partial persistence of benefit over the 12-month period.

Table 5: VAS scores at baseline and follow-up

Time point	VAS (Min–Max)	Mean ± SD	Mean difference vs baseline	*P* value
Initial visit	6.00–9.30	7.46 ± 0.91	–	–
12 weeks	5.00–8.30	6.41 ± 0.74	1.052	<0.001**
24 weeks	5.00–8.00	6.44 ± 0.64	1.028	<0.001**
1 year	5.80–9.00	7.16 ± 0.73	0.300	0.019*

* Moderately significant ($0.01 < P \leq 0.05$); ** strongly significant ($P \leq 0.01$).

Functional Assessment – Oswestry Pain/Disability Scores

At baseline, patients had a mean Oswestry score of 42.28 ± 11.49 (range 22.00–62.00), consistent with moderate functional disability. Following zoledronic

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acid infusion, there was a small but statistically significant improvement at the intermediate follow-up visits.

At 12 weeks, the mean Oswestry score decreased to 41.20 ± 10.35 (mean improvement vs baseline 1.080; t = 2.875; P = 0.006), and at 24 weeks it further reduced to 40.00 ± 9.78 (mean improvement 2.280; t = 5.027; P < 0.001). However, this improvement was not sustained at 1 year, when the mean score was 41.48 ± 9.76 (range 22.00–62.00), corresponding to a modest 0.800-point reduction from baseline that did not reach statistical significance (t = 1.639; P = 0.108). Thus, functional gains observed at 12 and 24 weeks were not maintained at 12 months.

Table 6: Oswestry pain scores at baseline and follow-up

Time point	Oswestry score (Min–Max)	Mean ± SD	Mean difference vs baseline	*P* value
Initial visit	22.00–62.00	42.28 ± 11.49	–	–
12 weeks	22.00–62.00	41.20 ± 10.35	1.080	0.006**
24 weeks	20.00–58.00	40.00 ± 9.78	2.280	<0.001**
1 year	22.00–62.00	41.48 ± 9.76	0.800	0.108

**Strongly significant (P ≤ 0.01).

DISCUSSION

This prospective study evaluated the impact of a single 5 mg intravenous zoledronic acid infusion on pain, function and lumbar spine BMD in adults over 40 years presenting with back pain and DXA-confirmed vertebral osteoporosis. The key findings were: (i) a high proportion (41.7%) of screened back-pain patients were osteoporotic; (ii) there was a clear female predominance and peak age between 51–60 years; (iii) vertebral deformities were more frequent in the lumbar than thoracic spine, especially at L1; (iv) lumbar spine BMD remained essentially stable over one year; and (v) pain scores improved significantly at 12 and 24 weeks, with partial loss of effect at one year, while functional gains on the Oswestry index were modest and not sustained. These results suggest that once-yearly zoledronic acid offers fracture-preventive therapy with short- to medium-term analgesic benefit, but is unlikely to be sufficient as a stand-alone strategy for long-term functional improvement [11- 13].

Osteoporosis as an under-recognised cause of back pain

In this back-pain cohort aged ≥40 years, 41.7% of patients screened by DXA were osteoporotic. This proportion is substantially higher than estimates for the general Indian adult population, where Babhulkar and Seth reported osteoporosis in 19.4% of adults and 33.1% of postmenopausal women in a nationwide sample of 31,238 individuals [14]. The enrichment seen in our study reflects targeted recruitment of symptomatic patients with persistent back pain, similar to hospital-based series where osteoporosis "presenting as low backache" has been emphasised as a frequent and often overlooked diagnosis.

Our findings align with neurosurgical and orthopaedic clinics where a high burden of low bone mass is reported among patients with back pain or spinal pathology. Sarmast et al. [12] found that all 100 patients in a neurosurgical clinic with low backache and DEXA-confirmed osteoporosis had clinically relevant risk factors, and concluded that osteoporosis as a cause of backache is not uncommon to be missed. Zaman et al. similarly showed that DEXA is an effective tool to detect osteoporosis early in patients hospitalised with chronic low back pain, particularly in postmenopausal women [13]. Indian surgical cohorts, Dave et al. reported that 65.5% of patients undergoing spinal procedures and 38.5% of those undergoing arthroplasty had osteoporosis, underlining the importance of systematic bone health assessment in spine-related practice [15]. Against this background, the observed 41.7% prevalence of osteoporosis among adult's ≥40 years with back pain in our study is biologically plausible and clinically important. It reinforces that persistent back pain in mid-life and older adults should trigger active evaluation for underlying osteoporosis, rather than being attributed solely to degenerative spine disease or muscular strain.

Demographic pattern: female predominance and peak in the fifth and sixth decades

Consistent with global epidemiology, our osteoporotic cohort showed a female preponderance (60%) with the highest concentration of patients in the 51–60-year age group [16]. This matches large Indian and international datasets where osteoporosis is more prevalent in women, particularly after menopause, and increases with age. Gender-specific age distribution in our sample demonstrated that both women and men were mainly clustered between 51–60 years, although women were more often represented at older ages (including 71–80 years), reflecting the combined impact of postmenopausal bone loss and longer female life expectancy. Similar age–sex patterns have been reported in Indian DEXA-based studies and global meta-analyses. This supports the external validity of our cohort and highlights the need for proactive osteoporosis screening in both sexes once chronic back pain develops in the fifth decade.

Vertebral morphometry: lumbar spine predominance of deformity

Lateral vertebral assessment showed relatively preserved thoracic vertebrae, with deformities predominantly affecting T6, T11 and T12, whereas lumbar deformities were more frequent, especially at L1 and L4. Overall, L1 was the most commonly abnormal level (32% deformed), followed by L4 and

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L2. This pattern is in keeping with established epidemiology of osteoporotic vertebral fractures. Multiple radiographic series have shown a bimodal distribution, with clusters in the mid-thoracic region and at the thoracolumbar junction (T12–L1) [17, 18]. Wang and colleagues similarly reported that L1, T12 and L2 were the most frequently fractured vertebrae in osteoporotic compression fractures [19]. Our higher frequency of deformities at L1, along with abnormalities at T11–T12 and L4, therefore mirrors the typical distribution of osteoporotic vertebral damage.

The use of lateral vertebral assessment is strength of this study. Vertebral fractures are often underdiagnosed on plain radiographs and in routine clinical practice [20, 21]. Morphometric techniques improve detection of mild and moderate deformities, which have prognostic importance because prevalent vertebral fractures strongly predict future fracture risk and chronic pain. The predominance of mild–moderate deformities in our cohort, and the relative rarity of severe compression, suggests a window of opportunity for early intervention to prevent progression.

Lumbar BMD response: stabilisation rather than clear gain

The mean AP lumbar spine BMD showed only a minimal absolute change over one year (from 0.7526 to 0.7542 g/cm²), with a slight shift of patients into higher BMD categories. Although this does not mirror the larger BMD gains reported in major phase III trials of zoledronic acid, the absence of further decline is clinically relevant, particularly given that untreated postmenopausal women typically lose 1–3% of spinal BMD per year, with greater losses in older individuals and those with comorbidities [22]. In the HORIZON Pivotal Fracture Trial, once-yearly 5 mg zoledronic acid for three years significantly reduced vertebral, hip and non-vertebral fractures and increased lumbar spine BMD by approximately 6–7% versus placebo [23], and similar fracture protection and BMD gains have been demonstrated in women following hip fracture and in pooled analyses across different risk strata [24]. The more modest densitometric response observed in our cohort may be attributed to several factors: (i) the relatively small sample size (n = 50) and assessment at a single skeletal site, limiting power to detect small changes beyond normal DXA variability; (ii) the exclusive use of lumbar spine measurements, where degenerative changes, osteophytes and aortic calcification may artefactually elevate BMD and obscure true gains or losses, whereas hip BMD or trabecular bone score might have provided a clearer signal; (iii) more advanced baseline disease, with established vertebral deformities and chronic back pain, in contrast to the generally healthier populations enrolled in pivotal trials; and (iv) the shorter follow-up period, as we evaluated BMD at 12 months after a single infusion, whereas cumulative benefits are more evident over three years in randomized controlled trials [25]. Taken together, these findings suggest that, in this high-risk symptomatic population where the expected natural course is progressive bone loss, simple stabilisation of lumbar spine BMD over one year is clinically meaningful and consistent with the known antiresorptive effects of zoledronic acid.

Pain outcomes: short- and medium-term benefit with partial attenuation

Pain intensity improved significantly at 12 and 24 weeks, with mean VAS reductions of about 1 point from baseline, but the effect waned by one year, although pain remained modestly lower than at enrolment. The magnitude of improvement is in the small-to-moderate range and likely clinically perceptible for many patients, especially in the first six months.

These findings parallel, but are somewhat smaller than, results from randomised trials of zoledronic acid in chronic low back pain. Koivisto et al. reported that a single 5 mg infusion significantly reduced VAS pain scores and NSAID use compared with placebo in patients with chronic low back pain and Modic changes, with the largest benefit seen at one month and a persisting effect up to one year [26]. In that study, the between-group difference in pain at one month was approximately 1.5 points on a 10-cm VAS, larger than the within-patient change observed in our cohort.

Indian observational series focused on osteoporotic back pain have also described meaningful pain relief after zoledronic acid. Parikh et al. and Uppin et al. documented statistically and clinically significant VAS and Oswestry/ODI improvements over six months following a single infusion in patients with osteoporosis-related back pain [27, 28]. Umesh et al. [29] similarly found that zoledronic acid improved pain and functional outcomes in patients with vertebral osteoporosis in a prospective cohort. Our one-year data suggest that analgesic benefits may be most pronounced in the first six months, with partial attenuation over time an effect consistent with both fracture-healing dynamics and the time course of bisphosphonate action on bone turnover.

Several explanations may account for the modest and transient nature of functional gains in this study. The Oswestry scores improved significantly at 12 and 24 weeks but returned close to baseline by one year. Disability in chronic back pain is multifactorial; vertebral osteoporosis and microfractures are only one component alongside degenerative disc disease, facet arthropathy, muscular deconditioning and psychosocial factors [30]. Moreover, our protocol intentionally avoided systemic analgesics after infusion to avoid confounding pain assessment; in real-world practice, combined pharmacological and rehabilitative strategies could yield larger functional improvements.

In contrast, trials where zoledronic acid is used in combination with percutaneous kyphoplasty for osteoporotic compression fractures report greater and more sustained reductions in VAS and ODI

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scores than surgery alone [31]. This suggests that in settings of acute or subacute vertebral collapse, the anti-fracture and antiresorptive actions of zoledronic acid translate more directly into symptomatic benefit. Our cohort, by design, included a broader spectrum of chronic back-pain patients with both subtle and overt vertebral deformity, which may dilute measurable functional gains.

Mechanistic considerations: beyond bone density

The analgesic effect of zoledronic acid in vertebral osteoporosis is probably mediated by more than just BMD stabilisation. Bisphosphonates inhibit osteoclast-mediated resorption, reduce bone turnover, and may stabilise microfractures within vertebral bodies, thereby reducing nociceptive input from the skeleton. Experimental and clinical data also suggest modulation of inflammatory pathways. In biomarker analyses from the Modic-change RCT, Koivisto et al. showed that zoledronic acid alters several circulating inflammatory mediators and bone-turnover markers over time, potentially influencing pain processing [32].

Our observation that pain improvement was most evident at 12–24 weeks, with partial attenuation at one year, is consistent with a scenario in which early suppression of bone turnover and microfracture activity reduces pain, but structural degenerative changes and non-osteoporotic generators of back pain remain unmodified. The incomplete and non-sustained change in Oswestry scores supports this interpretation.

Osteoporosis, degenerative spine disease and back pain: a complex interplay

Not all chronic back pain in osteoporotic patients arises from osteoporotic vertebral fractures alone. Recent work by Iwata et al. highlighted the intertwined roles of osteoporosis, vertebral fractures and degenerative spinal disorders in determining low back pain severity and functional limitation in older adults [30]. Even when osteoporosis is present, disc degeneration, facet arthropathy and spinal stenosis may be dominant pain drivers in a given individual.

In our study, patients with clear MRI evidence of degenerative disc disease were excluded where such imaging was available, but MRI was not performed uniformly. It is therefore likely that some included patients had mixed pathologies. This may help explain why vertebral deformities were relatively common while pain and disability improvements remained modest. Zoledronic acid can address the osteoporotic component but cannot reverse chronic degenerative changes.

Comparison with fracture-prevention literature and broader clinical value

Although fracture outcomes were not assessed in the present study, the choice of zoledronic acid as the therapeutic agent is supported by robust evidence from large RCTs. The HORIZON Pivotal Fracture Trial showed that once-yearly 5 mg zoledronic acid over three years reduced vertebral fractures by 70%, hip fractures by 41% and non-vertebral fractures by 25% compared with placebo In patients after hip fracture, zoledronic acid reduced new clinical fractures and was associated with improved survival. Meta-analyses of randomised trials confirm significant reductions in fracture incidence and, at some follow-up intervals, in mortality.

Thus, even though our one-year BMD change was small and pain benefits were modest, the use of zoledronic acid in this high-risk back-pain cohort is justified by its proven anti-fracture efficacy and convenient once-yearly dosing, which improves adherence compared with oral bisphosphonates. Current osteoporosis treatment guidelines also recognise intravenous zoledronic acid as an appropriate first-line or alternative therapy in patients at high fracture risk, or in those unable to tolerate or adhere to oral agents [33].

From a practical standpoint, our data support a dual message: (i) chronic back pain in patients over 40 years warrants active case-finding for osteoporosis using DXA and vertebral morphometry, and (ii) once-yearly zoledronic acid should be considered primarily as fracture-prevention therapy in such patients, with the expectation of some short-term pain relief but only limited long-term functional change unless combined with broader multimodal management.

Strengths and limitations

Strengths of this study include its prospective design, clearly defined inclusion and exclusion criteria, uniform dosing regimen (single 5 mg infusion), systematic use of validated outcome measures (VAS and modified Oswestry), and incorporation of both densitometric (DXA) and morphometric vertebral assessments. The restriction of systemic analgesics after infusion reduced pharmacological confounding of pain scores and provides a conservative estimate of the drug's direct analgesic effect. However, several limitations must be acknowledged. The study lacked a control or comparator group, preventing definitive attribution of observed changes solely to zoledronic acid and raising the possibility that part of the improvement reflects regression to the mean or natural fluctuation of symptoms. The sample size (n=50) limits statistical power, especially for detecting small changes in BMD. DXA measurements were confined to the AP lumbar spine, where degenerative changes can obscure true bone-density trends; hip or whole-body measurements were not available [31-33]. Vertebral fractures were graded morphometrically but not correlated with incident fracture events or radiographic progression over time. MRI was not performed in all patients, so residual confounding by degenerative disc disease or other spinal pathologies cannot be excluded. Finally, the one-year follow-up, although clinically relevant, may be insufficient to capture the full structural benefits of zoledronic acid, which accrue over several years in most RCTs.

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CONCLUSION

In adults over 40 years with back pain and DXA-confirmed vertebral osteoporosis, a single 5 mg intravenous infusion of zoledronic acid was associated with stabilisation of lumbar spine BMD over one year, modest but statistically significant reductions in pain at 12 and 24 weeks with partial persistence at one year, and only small, non-sustained improvements in functional disability. The high prevalence of osteoporosis among screened back-pain patients, the predominance of lumbar vertebral deformities, and the known anti-fracture efficacy of zoledronic acid together support routine bone-health evaluation and early initiation of potent antiresorptive therapy in this population. However, zoledronic acid alone is unlikely to normalise pain or disability, and should be integrated into a comprehensive, multimodal strategy for managing chronic back pain in patients with vertebral osteoporosis.

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