EPH138

Osteogenesis Imperfecta: Epidemiology Characteristics and Disease Burden in Two Real-world Databases

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INTRODUCTION

- Osteogenesis imperfecta (OI) is a hereditary, lifelong, systemic connective tissue disorder commonly characterized by low bone mineral density, bone fragility (brittle bones), recurrent fractures, and growth deficiency[1,2]
  - The incidence rate of OI ranges from 1:15,000 to 1:20,000 births worldwide
- OI Types I-IV vary in severity, with specific genetic inheritance based on clinical symptoms and radiographic features[1-3]
  - Additional phenotypic features such as blue sclerae, dentinogenesis imperfecta, hearing loss, joint hypermobility, pulmonary function impairment, cardiac valve abnormalities, and muscle weakness can vary according to OI type
- Treatment options are primarily supportive and symptomatic to prevent bone fractures, increase bone mass, and control symptom progression[3]
- There is a paucity of population-based studies that describe treatment patterns and disease burden for patients with OI in the real-world

OBJECTIVES

- To examine the characteristics and disease burden of OI in the United States (US) using two real-world healthcare databases

METHODS

Data Sources

- This retrospective cohort study included all patients registered in the IQVIA PharMetrics® Plus and TriNetX real-world databases
  - PharMetrics Plus: US closed-source, administrative database containing adjudicated medical and pharmacy claims and patient enrollment data derived from health insurance providers, revealing nearly all patients' healthcare activities during a specific enrollment period
  - TriNetX: US-based electronic medical records (EMR) database that collects EMR data directly from physicians to record details of patient encounters

Study Population

- Patients were included in this study if they had ≥ 2 ICD 10 diagnosis codes of OI (Q78.0) ≥ 30 days apart and had ≥ 12 months of continuous insurance enrollment between 01 October 2016 and 30 September 2021 (5-year study period). The observed date of the second OI diagnosis was defined as the index date to calculate the age at diagnosis

Treatment History

- National Drug Codes and Healthcare Common Procedure Coding System codes were used to identify main treatments for OI including bisphosphonates (BPs; oral and intravenous), denosumab, romosozumab, and teriparatide. Patients prescribed any of these medications during the study period were defined as having OI treatment

Fracture Rates

- Claims with fractures (excluding skull/face fractures) using ICD-10 codes were identified, and patients with ≥ 1 fracture claim in either database during the study period were considered as having a fracture event

Statistical Analysis

- Demographic characteristics of eligible OI patients, including age at diagnosis and gender, were analyzed descriptively. Main OI treatment methods, treatment rates, and fracture rates were described by age and gender. Additionally, chi-square tests were performed to compare fracture rates and treatment rates between different groups (*eg*, males vs females) using the PharMetrics Plus database. Statistical analyses were performed using the IQVIA E360 Platform for PharMetrics Plus database and R version 4.2.0, as well as the TriNetX, LLC Platform and EMR data

RESULTS

Patient Demographics by Age and Gender

- A total of 2178 unique patients with OI were identified in the PharMetrics Plus database, of which 55.9% were female **(Table 1)**
  - The proportion of female patients with OI was higher in the older age groups
- At index, 32.7% of patients were children or adolescents (< 18 years)
- Approximately one-third (32.7%) of patients < 18 years had a confirmed diagnosis of OI during their childhood
  - Fewer patients with OI were diagnosed at age 18–26 and ≥ 65 years, potentially due to insurance switching

Table 1. Gender by Age at Index Date

Age at Index Date[a]	Total (%)	Female (%)	Male (%)
Total	2178 (100)	1218 (55.9)	960 (44.1)
≤1 year	64 (2.9)	27 (42.2)	37 (57.8)
2–4 years	113 (5.2)	58 (51.3)	55 (48.7)
5–17 years	536 (24.6)	250 (46.6)	286 (53.4)
18–26 years	296 (13.6)	174 (58.8)	122 (41.2)
27–45 years	548 (25.2)	338 (61.7)	210 (38.3)
46–64 years	543 (24.9)	320 (58.9)	223 (41.1)
≥65 years	78 (3.6)	51 (65.4)	27 (34.6)

[a]Index date: the observed date of the 2nd diagnosis of OI (ICD-10: Q78.0); Source: IQVIA PharMetrics Plus (01-Oct-2016 to 30-Sep-2021).

Treatment History

- Among 27.4% (n = 596) treated patients, bisphosphonates (n = 544, 25.0%) were most commonly used to manage OI during an average 3.6 years of enrollment over the 5-year study period **(Table 2)**
- Treatment rates varied by the patients' age at diagnosis:
  - Children with a confirmed diagnosis between 2–4 years old had the highest treatment rate (n = 54, 47.8%)
  - Treatment rates increased for patients diagnosed at age ≥ 46 years, with an increased use of denosumab and oral BPs in this age group, indicating possible concomitant treatment for osteoporosis

Table 2. Treatment of OI by Age Group

Treatments		Any Treatments	BPs			Denosumab	Other Treatments[a]
			Any BPs	Oral	IV		
Age at Index	**Total (%)[b]**	**596 (27.4)**	**544 (25.0)**	**168 (7.7)**	**384 (17.6)**	**65 (3.0)**	**1 (<0.1)**
≤1 yr	64 (2.9)	27 (42.2)	27 (42.2)	0 (0)	27 (42.2)	0 (0)	0 (0)
2–4 yrs	113 (5.2)	54 (47.8)	54 (47.8)	0 (0)	54 (47.8)	0 (0)	0 (0)
5–17 yrs	536 (24.6)	206 (38.4)	205 (38.2)	21 (3.9)	186 (34.7)	1 (0.2)	0 (0)
18–26 yrs	296 (13.6)	39 (13.2)	39 (13.2)	6 (2.0)	35 (11.8)	1 (0.3)	0 (0)
27–45 yrs	548 (25.2)	72 (13.1)	63 (11.5)	39 (7.1)	26 (4.7)	10 (1.8)	0 (0)
46–64 yrs	543 (24.9)	166 (30.6)	134 (24.7)	86 (15.8)	50 (9.2)	40 (7.4)	0 (0)
≥65 yrs	78 (3.6)	32 (41.0)	22 (28.2)	16 (20.5)	6 (7.7)	13 (16.7)	1 (1.3)

[a]Other treatments include romosozumab and teriparatide. [b]Denominator N = 2178.
BP, bisphosphonate; IV, intravenous; yr, year.

Fracture Rates

- In total, 55.9% (n = 1218) of patients with OI had ≥ 1 fracture diagnosis claim during the 5-year study period, among whom 15.7% (n = 191) were on BPs before the first fracture
  - The mean number of fracture claims per patient-year was 5
- Within the study population, children had higher higher fracture rates than adults (73.2% of all children; 47.5% of all adults; $P < 0.05$; **Figure 1**)
- Males had similar fracture rates as females (58.0 vs 54.3%, respectively; $P = 0.09$)
- Patients with fracture histories had higher treatment rates than those without (34.9% vs 17.8%, $P < 0.05$; **Figure 2**)

Figure 1. Fracture Rates by Age and Gender

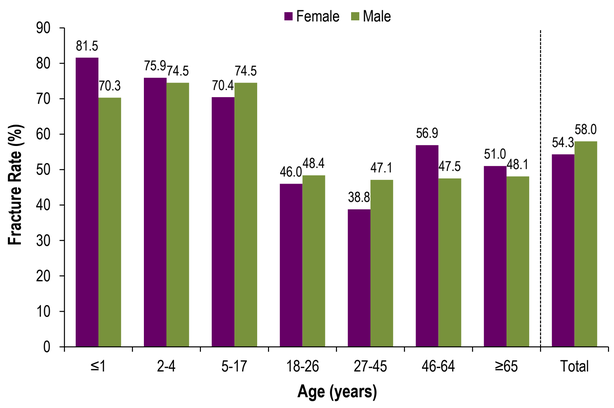
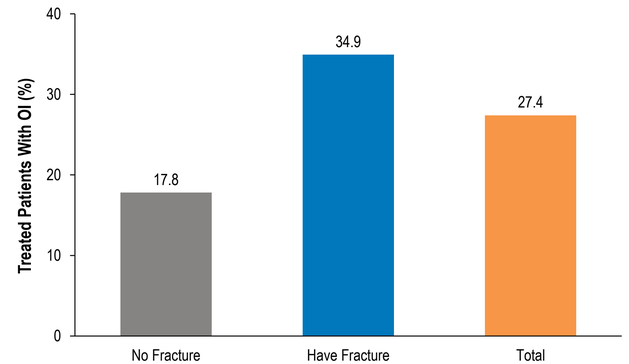


Figure 2. Treatment Rate by Fracture History



EMR Database Results

- In total, 4300 patients with OI were identified using the TriNetX database:
  - Among 24.2% (n = 1041) treated patients, bisphosphonates (n = 946, 22.0%) were most commonly used to manage patients with OI
  - 55.7% (n = 2395) had ≥1 fracture diagnosis during the study period
- These results are similar to the results observed from the PharMetrics Plus commercial claims database

LIMITATIONS

- There is no validated algorithm to identify patients with OI using ICD-10 codes; however, our algorithm required two ICD-10 codes at least 30 days apart to minimize misclassifications, and yielded similar results from two different real-world databases
- It is possible that patients are misclassified as having OI or not having OI due to misdiagnosis or failure to correctly identify patients with the ICD-10 diagnosis codes
- Different subtypes of OI, thus severity, could not be differentiated using ICD-10 codes in claims data

CONCLUSIONS

- Most patients with OI had ≥ 1 fracture during the study period
- Children had higher fracture rates than adults. Treatment rates were low and varied by age
- Bisphosphonates were the most utilized treatment for the management of OI; however, a third of treated patients still had a history of fractures
- These results highlight a high unmet medical need for a safe and effective treatment that reduces the incidence of fractures and prevents the long-term consequences of OI

REFERENCES

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