

**RESEARCH ARTICLE**

# Descriptive Epidemiology and Survival Rate of Osteosarcoma: The First National Population-Based Study in the Middle East (2008-2014)

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Received: 23 August 2021

Accepted: 3 July 2023

**Abstract**

**Objectives:** The epidemiology of osteosarcoma (OS), the most common primary bone sarcoma, was not evaluated in the Middle East. Therefore, this study aimed to examine the incidence, demographic characteristics, epidemiology, and survival rate of patients with different subtypes of OS, based on data derived from the Iran National Cancer Registry (INCR) to evaluate the influence of ethnicity and race.

**Methods:** All OS patients registered in the INCR between March 20, 2008, and March 20, 2014, were enrolled in this study, and information such as age, gender, cancer location, OS subtype, and survival time were evaluated statistically.

**Results:** The Age-Standardized Incidence Rate (ASIR) for OS was 3.02 per million person-years, with a mean age of 25.6 years and a male-female ratio of 1.54:1. Not Otherwise Specified (NOS) OS, chondroblastic OS, and central OS had the highest frequencies among the subtypes of OS. The overall one-, three-, and five-year survival rates were 87%, 61%, and 49%, respectively, with a mean duration of 6.16 years.

**Conclusion:** The ASIR of OS in our country was similar to that in the US and higher than that in China. The peak frequency was between 15-19 years old. The male-female ratio in our patients was higher than the OS gender ratio in most series. Although it was not statistically significant, older age at the time of diagnosis, axial location, and male gender were the poorest prognosis factors.

**Level of evidence:** III

**Keywords:** Bone cancer, Epidemiology Incidence, Osteosarcoma, Survival

**Introduction**

Osteosarcoma (OS) is the most common primary malignant tumor of the bone, characterized by mesenchymal-originated spindle cells depositing the immature osteoid matrix.<sup>1-5</sup> It includes distinct morphology subtypes with diverse clinical behaviors.

The age distribution is bimodal, with the initial major peak occurring during the second decade of life, followed by a much smaller peak in patients older than 60.<sup>2,6,7</sup> With an annual incidence rate of 3.1 cases per million in the US, OS accounts for less than 1% of all newly diagnosed cancers in adults and 3-5% in children.<sup>5</sup>

The metaphyseal region of long tubular bones is the most prevalent location for OS involvement. Therefore, the distal femur, proximal tibia, and proximal humerus are the most involved in descending order. OS in the axial skeleton increases in frequency with age, with 40% of patients being above 60 years and less than 12% below 24 years.<sup>3,8</sup> OS in elderly patients is often secondary to the sarcomatous transformation of Paget's disease of the bone, irradiated bone, or some other benign bone disorders. The male gender has been reported to be affected more frequently, and the incidence of OS in African-Americans is slightly

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higher than in Caucasians. In China, the annual incidence of OS was much lower than in the US, with only 0.5 patients per million.<sup>8</sup>

The survival rate for OS has remained below 70% for localized disease and below 20% in patients with metastasis for decades despite ongoing studies.<sup>9,10</sup> the incidence and mortality patterns of OS have been rarely studied in non-western countries and never in the Middle East.

This study aimed to examine the incidence, demographic characteristics, epidemiology, and survival rate of patients with different subtypes of OS, based on data derived from the Iran National Cancer Registry (INCR)<sup>11</sup> to evaluate the influence of ethnicity and race on the most common primary bone sarcoma.

### Materials and Methods

This national population-based cancer registry study was based on all patients affected by OS registered in the INCR between March 20, 2008, and March 20, 2014. Only microscopically and pathologically confirmed cases of OS were enrolled in this study. Since the INCR is a subdivision of the Ministry of Health and Medical Education in Iran, the registered data cover nearly all diagnosed cases in the population during these six years. Patients with metastatic OS at presentation were excluded from the study. All primary OS cases were classified in conformance with the International Classification of Diseases for Oncology.<sup>12</sup>

Variables such as age, gender, cancer location, and OS subtype were collected from the medical records of these patients. All primary OS cases (primary site codes C40.0-40.9 and C41.0-41.9 and histology codes 9180-9187 and 9192-9195) were included in these analyses. Additional detailed site descriptions, including specific bones or epiphyseal, metaphyseal, and diaphyseal locations, were not available. Death due to OS and the interval between diagnoses and death were registered as survival times.

Descriptive statistics were expressed as several new cases (percentages) and the mean age (standard deviation [SD]) for all morphology types of OS, including not otherwise specified (NOS) OS, chondroblastic, fibroblastic, and telangiectatic OS, OS in Paget's disease of the bone, small cell OS, central OS, as well as intraosseous well-differentiated, parosteal, periosteal, high-grade surface, and intracortical OS. The frequency of males and females was compared using the binomial proportion test.

The age-standardized incidence rate (ASIR) was calculated directly using the new WHO standard population. The 95% confidence interval (CI) was obtained using a direct method

for all ASIRs among males and females. Furthermore, the age-specific incidence rate was calculated for each age group, age decade, gender, and the three largest morphology groups.<sup>13,14</sup>

The cumulative survival rate for total cases and each c-code was estimated using the Kaplan-Meier survival curve. The one-, three-, five-, and seven-year survival rates, the mean survival time (year), and the median survival time (year) were calculated for each variable. All analyses were conducted using SPSS (version 26), and a P-value of less than 0.05 was considered the significance level.

### Results

A total of 1736 OS patients were included in this study, and duplicate analysis was performed to remove completely identical records from the data. About 5% of the cases were identified as duplicate records and were excluded [Table 1].

Year	Before duplicate extraction	After duplicate extraction	Percentage
2008	221	220	0.45%
2009	203	202	0.49%
2010	199	198	0.50%
2011	314	291	7.32%
2012	286	252	11.89%
2013	289	263	9.00%
2014	224	223	0.45%
Total	1736	1649	5.01%

Out of 1649 OS patients with a mean age of 25.6 years, 1002 (60.8%) cases were male (mean age: 25.4 years), and 647 cases were female (mean age: 25.8 years). The NOS OS, chondroblastic OS, and central OS had the highest frequencies of 1220 (males: 61.9%, females: 38.1%), 175 (males: 62.9%, females: 37.1%), and 102 cases (males: 61.8%, females: 38.2%), respectively. The relationship between these three morphology types and gender was significant ( $P$ -value<0.05), and males were afflicted more frequently than females. The mean age of these groups was about 22-26 years, with a non-significant difference between males and females ( $P$ -value>0.05). Other morphology types accounted for only 9.22% (7.39% of males, 12.06% of females) of total cases, in which the frequency and mean age were not significantly different between genders [Table 2].

M-Code	Morphology Type	Number of New Cases (Percentage)			Mean Age (Standard Deviation)			ASIR (95% Confidence Interval)		
		Total	Male	Female	Total	Male	Female	Total	Male	Female
9180	Osteosarcoma NOS**	1220	755 (61.9)	465 (38.1)	25.6 (16.3)	25.7 (16.1)	25.4 (16.6)	2.26 (2.13-2.39)	2.75 (2.55-2.95)	1.76 (1.60-1.93)
9181	Chondroblastic osteosarcoma**	175	110 (62.9)	65 (37.1)	25.8 (14.3)	24.4 (12.3)	28.2 (17.1)	0.31 (0.26-0.36)	0.38 (0.31-0.45)	0.24 (0.18-0.30)

Table 2. Continued										
9182	<b>Fibroblastic osteosarcoma</b>	18	9 (50.0)	9 (50.0)	26.7 (15.6)	24.1 (8.2)	29.2 (20.9)	0.03 (0.02-0.05)	0.03 (0.01-0.05)	0.04 (0.01-0.06)
9183	<b>Telangiectatic osteosarcoma</b>	34	19 (55.9)	15 (44.1)	22.2 (11.8)	22.6 (12.6)	21.6 (11.1)	0.06 (0.04-0.08)	0.07 (0.04-0.10)	0.05 (0.03-0.08)
9184	<b>Osteosarcoma in Paget disease of bone</b>	----	----	----	----	----	----	----	----	----
9185	<b>Small cell osteosarcoma</b>	17	9 (52.9)	8 (47.1)	20.0 (9.1)	17.1 (6.5)	23.3 (10.8)	0.03 (0.02-0.04)	0.03 (0.01-0.05)	0.03 (0.01-0.05)
9186	<b>Central osteosarcoma*</b>	102	63 (61.8)	39 (38.2)	23.7 (15.0)	22.8 (12.7)	25.2 (18.1)	0.19 (0.15-0.22)	0.23 (0.17-0.28)	0.14 (0.10-0.19)
9187	<b>Intraosseous well-differentiated osteosarcoma</b>	6	5 (83.3)	1 (16.7)	25.0 (12.1)	23.4 (12.8)	33.0 (0.0)	0.01 (0.00-0.02)	0.02 (0.00-0.03)	0.00 (0.00-0.01)
9192	<b>Parosteal osteosarcoma</b>	64	24 (37.5)	40 (62.5)	28.6 (10.7)	29.8 (13.8)	27.9 (8.4)	0.11 (0.08-0.13)	0.08 (0.05-0.12)	0.13 (0.09-0.17)
9193	<b>Periosteal osteosarcoma</b>	8	4 (50.0)	4 (50.0)	21.3 (9.3)	17.0 (5.9)	25.5 (10.9)	0.01 (0.00-0.02)	0.01 (0.00-0.03)	0.01 (0.00-0.03)
9194	<b>High-grade surface osteosarcoma</b>	5	4 (80.0)	1 (20.0)	49.6 (32.6)	58.8 (29.3)	13.0 (0.0)	0.01 (0.00-0.02)	0.02 (0.00-0.04)	0.00 (0.00-0.01)
9195	<b>Intracortical osteosarcoma</b>	----	----	----	----	----	----	----	----	----
	<b>Total**</b>	1649	1002 (60.8)	647 (39.2)	25.6 (15.8)	25.4 (15.5)	25.8 (16.2)	3.02 (2.87-3.17)	3.62 (3.39-3.85)	2.41 (2.23-2.61)

\*\*=Binomial test for comparing the frequency of cancer in males and females with a P-value of less than 0.01

\*=Binomial test for comparing the frequency of cancer in males and females with a P-value of less than 0.05

The ASIR for total cases was 3.02 (95% CI: 2.87-3.17) per million person-years, while males and females had ASIRs of 3.62 (95% CI: 3.39-3.85) and 2.41 (95% CI: 2.23-2.61) per million, respectively. The NOS OS, the largest morphology group, had an ASIR of 2.26 (95% CI: 2.13-2.39) per million

person-years. Considering gender, the ASIR of NOS OS was 2.75 (95% CI: 2.55-2.95) and 1.76 (95% CI: 1.60-1.93) per million for males and females, respectively. Other ASIRs were less than 0.5 per million person-years among genders [Table 3].

Table 3. Number of new cases (age-specific incidence rate/per million person-years) for osteosarcoma, chondroblastic osteosarcoma, and central osteosarcoma, as well as total records during 2008-2014

Age (Decade)	Osteosarcoma			Chondroblastic osteosarcoma			Central osteosarcoma			Total		
	Total	Male	Female	Total	Male	Female	Total	Male	Female	Total	Male	Female
4-0	12 (0.27)	4 (0.18)	8 (0.37)	2 (0.05)	2 (0.09)	0 (0.00)	1 (0.02)	1 (0.04)	0 (0.00)	15 (0.34)	7 (0.31)	8 (0.37)
5-9	62 (1.53)	32 (1.55)	30 (1.51)	2 (0.05)	1 (0.05)	1 (0.05)	8 (0.20)	5 (0.24)	3 (0.15)	76 (1.88)	40 (1.94)	36 (1.82)

Table 3. Continued

<b>First</b>	74 (0.88)	36 (0.84)	38 (0.92)	4 (0.05)	3 (0.07)	1 (0.02)	9 (0.11)	6 (0.14)	3 (0.07)	91(1.08)	47 (1.09)	44 (1.06)
<b>10-14</b>	185 (4.50)	103 (4.93)	82 (4.06)	16 (0.39)	8 (0.38)	8 (0.40)	17 (0.41)	9 (0.43)	8 (0.40)	238 (5.80)	128 (6.13)	110 (5.45)
<b>15-19</b>	323 (6.83)*	215 (8.98)	108 (4.62)	50 (1.06)*	34 (1.42)	16 (0.68)	26 (0.55)*	19 (0.79)	7 (0.30)	429 (9.07)*	288 (12.03)	141 (6.03)
<b>Second</b>	508 (5.75)*	318 (7.10)	190 (4.36)	66 (0.75)*	42 (0.94)	24 (0.55)	43 (0.49)	28 (0.62)	15 (0.34)	667 (7.55)*	416 (9.28)	251 (5.76)
<b>20-24</b>	206 (3.61)*	147 (5.15)	59 (2.06)	41 (0.72)*	28 (0.98)	13 (0.45)	18 (0.32)	10 (0.35)	8 (0.28)	294 (5.15)*	201 (7.04)	93 (3.25)
<b>25-29</b>	116 (1.99)*	71 (2.42)	45 (1.55)	21 (0.36)	13 (0.44)	8 (0.28)	9 (0.15)	5 (0.17)	4 (0.14)	165 (2.82)*	96 (3.27)	69 (2.37)
<b>Third</b>	322 (2.79)*	218 (3.77)	104 (1.80)	62 (0.54)*	41 (0.71)	21 (0.36)	27 (0.23)	15 (0.26)	12 (0.21)	459 (3.97)*	297 (5.13)	162 (2.81)
<b>30-34</b>	54 (1.10)	26 (1.05)	28 (1.15)	8 (0.16)	4 (0.16)	4 (0.16)	8 (0.16)	5 (0.20)	3 (0.12)	91 (1.86)	43 (1.74)	48 (1.98)
<b>35-39</b>	47 (1.18)	23 (1.13)	24 (1.22)	8 (0.20)	6 (0.29)	2 (0.10)	3 (0.08)	2 (0.10)	1 (0.05)	66 (1.65)	34 (1.67)	32 (1.63)
<b>Forth</b>	101 (1.14)	49 (1.09)	52 (1.19)	16 (0.18)	10 (0.22)	6 (0.14)	11 (0.12)	7 (0.16)	4 (0.09)	157 (1.77)	77 (1.71)	80 (1.82)
<b>40-44</b>	47 (1.38)*	32 (1.85)	15 (0.89)	7 (0.20)	4 (0.23)	3 (0.18)	0 (0.00)	0 (0.00)	0 (0.00)	64 (1.87)	38 (2.20)	26 (1.54)
<b>45-49</b>	26 (0.91)	14 (0.97)	12 (0.85)	6 (0.21)	3 (0.21)	3 (0.21)	3 (0.10)	3 (0.21)	0 (0.00)	36 (1.26)	21 (1.46)	15 (1.06)
<b>Fifth</b>	73 (1.16)*	46 (1.45)	27 (0.87)	13 (0.21)	7 (0.22)	6 (0.19)	3 (0.05)	3 (0.09)	0 (0.00)	100 (1.59)	59 (1.86)	41 (1.32)
<b>50-54</b>	39 (1.61)	23 (1.90)	16 (1.32)	5 (0.21)	4 (0.33)	1 (0.08)	3 (0.12)	2 (0.17)	1 (0.08)	50 (2.07)	30 (2.48)	20 (1.66)
<b>55-59</b>	28 (1.52)	18 (1.97)	10 (1.07)	0 (0.00)	0 (0.00)	0 (0.00)	2 (0.11)	1 (0.11)	1 (0.11)	30 (1.62)	19 (2.08)	11 (1.18)
<b>Sixth</b>	67 (1.57)	41 (1.93)	26 (1.21)	5 (0.12)	4 (0.19)	1 (0.05)	5 (0.12)	3 (0.14)	2 (0.09)	80 (1.88)	49 (2.30)	31 (1.45)
<b>60-64</b>	22 (1.66)	12 (1.88)	10 (1.46)	2 (0.15)	1 (0.16)	1 (0.15)	2 (0.15)	1 (0.16)	1 (0.15)	29 (2.19)	17 (2.67)	12 (1.75)
<b>65-69</b>	20 (2.10)	14 (3.00)	6 (1.23)	4 (0.42)	2 (0.43)	2 (0.41)	0 (0.00)	0 (0.00)	0 (0.00)	25 (2.62)	16 (3.43)	9 (1.85)
<b>Seventh</b>	42 (1.84)	26 (2.35)	16 (1.36)	6 (0.26)	3 (0.27)	3 (0.26)	2 (0.09)	1 (0.09)	1 (0.09)	54 (2.37)	33 (2.99)	21 (1.79)
<b>70-74</b>	14 (1.78)	10 (2.51)	4 (1.03)	1 (0.13)	0 (0.00)	1 (0.26)	1 (0.13)	0 (0.00)	1 (0.26)	18 (2.29)	12 (3.01)	6 (1.55)
<b>75-79</b>	11 (1.80)	7 (2.20)	4 (1.37)	0 (0.00)	0 (0.00)	0 (0.00)	0 (0.00)	0 (0.00)	0 (0.00)	12 (1.97)	8 (2.52)	4 (1.37)

Table 3. Continued

<b>Eighth</b>	25 (1.79)	17 (2.37)	8 (1.18)	1 (0.07)	0 (0.00)	1 (0.15)	1 (0.07)	0 (0.00)	1 (0.15)	30 (2.15)	20 (2.79)	10 (1.47)
<b>80-85</b>	5 (1.48)	2 (1.21)	3 (1.75)	2 (0.59)	0 (0.00)	2 (1.17)	0 (0.00)	0 (0.00)	0 (0.00)	7 (2.08)	2 (1.21)	5 (2.92)
<b>+85</b>	3 (1.03)	2 (1.32)	1 (0.71)	0 (0.00)	0 (0.00)	0 (0.00)	1 (0.34)	0 (0.00)	1 (0.71)	4 (1.37)	2 (1.32)	2 (1.42)
<b>Total</b>	1220 (2.32)*	755 (2.85)	465 (1.78)	175 (0.33)*	110 (0.41)	65 (0.25)	102 (0.19)*	63 (0.24)	39 (0.15)	1649 (3.14)*	1002 (3.78)	647 (2.48)

\*=Binomial test for comparing the frequency of cancer in males and females with a P-value of less than 0.05

In the next step, the frequency and crude incidence rates were obtained for NOS OS, chondroblastic OS, central OS, and total patients in each age group and age decade. The results showed that the highest frequency was between 10 and 29 years, with 1126 cases (68.28% of total patients). The peak of frequency in NOS OS, chondroblastic OS, and central OS was in the 15-19 years age group with 323

(male: 215, female: 108), 50 (male: 34, female: 16), and 26 cases (male: 19, female: 7), respectively. Furthermore, the age-specific incidence rate in these three morphology types was 6.83, 1.06, and 0.55 per million person-years, respectively [Table 3]. The trend of ASIRs among males and females during 2008-2015 is curved in [Figure 1].

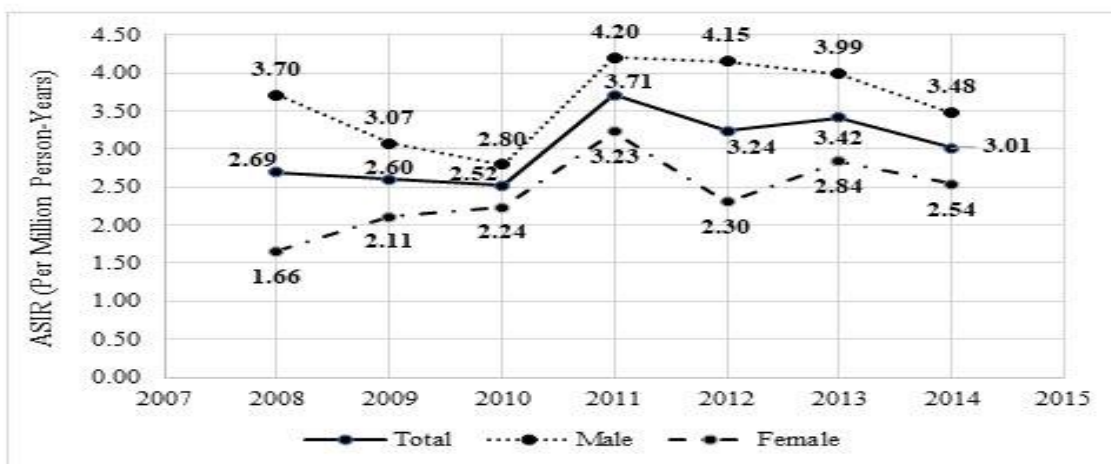


Figure 1. ASIR of osteosarcoma during 2008-2015 based on

In the current study, 289 cases were included in the survival analysis. The survival probability was estimated using the Kaplan-Meier curve. Based on the results, the cumulative survival was about 40% at the end of the study (after 125 months) for total patients; however, the survival probability for c-codes 40 and 41 was 41% and 32%, respectively [Figure 2]. Furthermore, the five-year survival rate was 0.51 (95% CI: 0.50-0.58) for c-code 40 and 0.41 (95% CI: 0.31-0.55) for c-code=41, and the mean survival time in c-codes 40 and 41 was 6.41 and 6.15 years, respectively [Table 4].

The overall one-, three-, and five-year survival rates were 0.87 (95% CI: 0.83-0.91), 0.61 (95% CI: 0.55-0.67), and

0.49 (95% CI: 0.43-0.60), respectively, with a mean duration of 6.16 (95% CI: 5.62-6.93) years. Among males, the five-year survival rate was 0.45 (95% CI: 0.38-0.53), while females had a five-year survival rate of 0.54 (95% CI: 0.46-0.63).

In addition, the mean survival time in females was about one year higher than that in males. The central OS had the lowest five-year survival rate, with a value of 0.25 (95% CI: 0.11-0.58). The difference in survival rates between variable levels was insignificant (log-rank  $P$ -value>0.05) [Table 4].

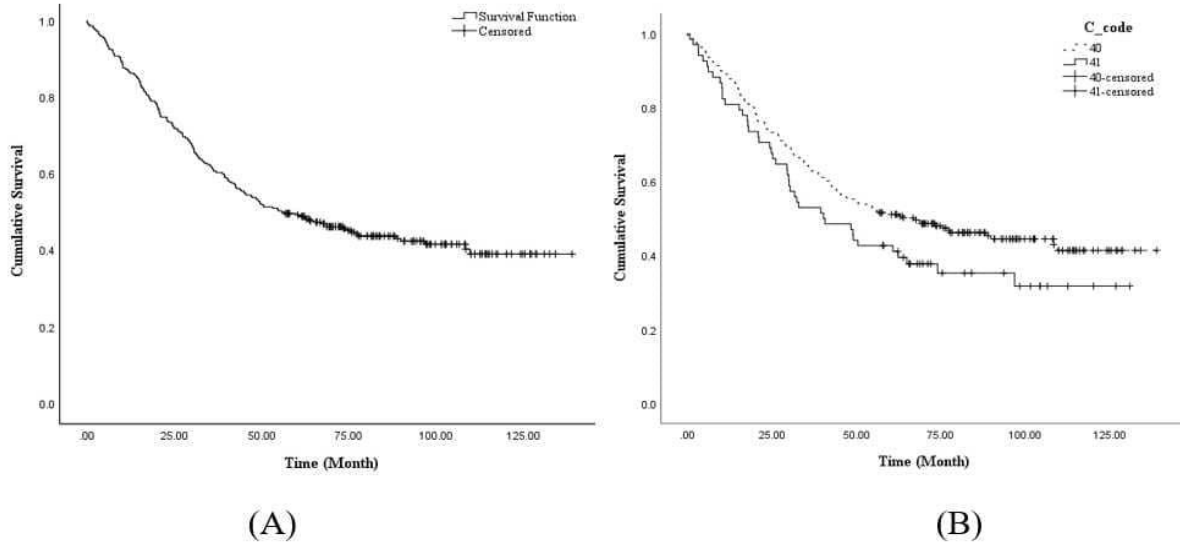


Figure 2. Kaplan-Meier plot for A) total osteosarcoma patients and B) each C-code=40 and 41

Table 4. Mean/median survival time (year) and one-, three-, five-, and seven-year survival rate by variable levels

Variable	C-Code	Survival Rate				Mean Survival Time (year) 95% CI	Median Survival Time (year) 95% CI
		One-Year Survival Rate 95% CI	Three-Year Survival Rate 95% CI	Five-Year Survival Rate 95% CI	Seven-Year Survival Rate 95% CI		
C-Code	40 (n=221)	0.88 (0.84-0.93)	0.63 (0.57-0.70)	0.51 (0.50-0.58)	0.46 (0.40-0.53)	6.41 (5.80-7.02)	5.50 (3.65-7.64)
	41 (n=68)	0.81 (0.72-0.91)	0.53 (0.42-0.66)	0.41 (0.31-0.55)	0.35 (0.25-0.49)	6.15 (4.14-6.16)	3.31 (1.87-4.75)
Sex	Male (n=166)	0.83 (0.78-0.89)	0.58 (0.51-0.66)	0.45 (0.38-0.53)	0.41 (0.34-0.49)	5.60 (4.93-6.26)	3.89 (2.62-5.16)
	Female (n=123)	0.91 (0.86-0.96)	0.64 (0.56-0.73)	0.54 (0.46-0.63)	0.47 (0.38-0.57)	6.66 (5.62-6.69)	6.01 (3.08-8.94)
M-Code	Osteosarcoma (n=205)	0.86 (0.82-0.91)	0.61 (0.54-0.68)	0.49 (0.43-0.57)	0.46 (0.39-0.53)	6.14 (5.52-6.75)	4.96 (2.15-7.41)
	Chondroblastic osteosarcoma (n=35)	0.83 (0.71-0.96)	0.60 (0.46-0.79)	0.46 (0.32-0.66)	0.32 (0.19-0.54)	5.58 (4.13-7.04)	4.37 (2.13-6.60)
	Central osteosarcoma (n=16)	0.81 (0.64-1.00)	0.50 (0.31-0.82)	0.25 (0.11-0.58)	---	3.08 (2.09-4.06)	2.51 (0.00-5.14)
Sum of Decade of Age	Second (n=121)	0.88 (0.82-0.94)	0.66 (0.58-0.75)	0.60 (0.50-0.67)	0.51 (0.43-0.61)	6.68 (5.90-7.46)	---
	Third (n=82)	0.89 (0.83-0.96)	0.63 (0.54-0.75)	0.46 (0.37-0.59)	0.44 (0.34-0.56)	4.65 (4.06-5.24)	4.14 (2.44-5.84)
	Sixth (n=14)	0.93 (0.80-1.00)	0.50 (0.30-0.84)	0.29 (0.13-0.65)	---	3.13 (2.20-4.05)	---
	Overall (n=289)	0.87 (0.83-0.91)	0.61 (0.55-0.67)	0.49 (0.43-0.60)	0.44 (0.38-0.50)	6.16 (5.62-6.93)	4.58 (3.17-5.98)



## Discussion

This analysis provides comprehensive information on the detailed epidemiology of primary OS based on data derived from the INCR.<sup>11</sup> Some registries in the US (SEER)<sup>15</sup> and England (NCIN)<sup>16</sup> provide general population data. Nevertheless, to evaluate the influence of race and ethnicity, regional registries worldwide help to study more genetically similar populations.

In our country, the ASIR for the total cases of OS was 3.02 per million person-years, which was similar to the incidence rate (3.1) in the US, as reported by Mirabello et al.,<sup>3</sup> but higher than that in China (0.5).<sup>8</sup>

Although previous studies accentuated bimodal frequency for OS incidence by age,<sup>3,6,15,17-19</sup> in our study, the peak frequency was in the second decade of life, especially 15-19 years (26% of cases), and its abundance was reduced with an increase in age such that the frequency was low in the seventh (1.8%) and eighth (0.6%) decades of life. Perhaps the cause of the low prevalence of OS in the elderly in our country is the rarity of Paget's disease in the Iranian race because, in previous studies,<sup>3,20,21</sup> a significant fraction of OS in elderly patients has been reported among those with Paget's disease.

OS is rare in children younger than five years, and only 2% of patients with OS were reported in this age group by Hartford<sup>19</sup>; likewise, in our patients, only 0.9% fell into this age group.

Differences in incidence rates by gender were significant in our patients. Male predominance was reported in most OS series.<sup>22-24</sup> Mirabello et al. also reported that OS is predominant in males in most countries.<sup>18</sup> The male-female ratio was 1.54:1 in our patients, which was higher than that in most series (1.22:1 was reported by Mirabello et al.).<sup>3</sup>

In contrast to many earlier reports that demonstrated slightly higher incidence rates of OS in females of each age stratum in the group aged <15 years than males in that age group,<sup>3,25,26</sup> in our patients, females had higher rates only in the stratum age of 0 to 4 years.

Before the 1970s, most patients died of metastatic disease, mainly of the lungs, with only a 20% five-year survival rate.<sup>27,28</sup> However, chemotherapy protocols led to a significant increase in overall survival rates.<sup>29,30</sup> Many previous studies attempted to identify the prognostic factors for OS, and their results were not approximate. The overall one-, three-, and five-year survival rates in our patients were 87%, 61%, and 49%, respectively.

Tempelaere et al. reported only 25% of the five-year survival rate in patients older than 50.<sup>31</sup> Bielback et al., in 2002, reported a poor prognosis in older patients due to increased axial distribution, distant disease at diagnosis, and decreased tolerance of high-dose chemotherapy.<sup>32</sup> In another study, a higher percentage of axial tumors was reported in patients aged 60 and above (39.7%) than in patients aged <25 (12.2%), and 34.3% of distant disease was reported in patients above 60 years in comparison with only 17.9% in patients aged <25 years.<sup>5</sup> Although it was not statistically significant, our study's five-year survival rate and mean survival time were 60% and 6.68 years, respectively, for patients in the second decade of life, which was higher than 29% and 3.13 years for patients in the sixth

decade of life. Concerning age, the five-year survival rate of our patients was similar to the National Cancer Data Base Report,<sup>33</sup> with a relative five-year survival rate of 60% for patients younger than 30 years, 50% for patients between 30 and 49 years, and 30% for patients 50 years and older.

Mankin et al. found no significant gender differences in the five-year survival rate (68%) for OS.<sup>30</sup> Although gender differences were not statistically significant in our study, the five-year survival rate and the mean survival time were 54% and 6.66 years, respectively, for female patients, which was higher than 45% (the five-year survival rate) and 5.6 years (the mean survival time) for male patients. A higher survival rate in the female gender was also reported in some previous studies.<sup>3,34</sup>

Patients with primary OS of the rib were reported to have a five-year survival rate of only 15%.<sup>35</sup> In more than 2000 patients in the EURAMOS-1 (European and American OS Study) cohort, the axial skeleton tumor site has been reported as an adverse factor for prognosis.<sup>36</sup> Although it was not statistically significant in our patients, the five-year survival rate for the axial skeleton as a primary site of OS was 41%, which was lower than 51% in the appendicular OS.

Our findings should be scrutinized in light of several limitations. In registry data, there is a probability of misclassification or miscoding, no information was provided about patients with metastatic disease at the presentation time, and information on the type of surgery was also limited. Despite these limitations, the current study is the first report on OS incidence in the Middle East. It provides an accurate impression of age, gender, race, and survival rate for primary OS incidence in Iran.

## Conclusion

The ASIR of OS in our country was 3.02 per million person-years, similar to the incidence rate in the US and higher than that in China. The three highest-frequency morphology groups were the NOS OS, chondroblastic OS, and central OS. The peak frequency was in the second decade of life, especially between 15-19 years. The male-female ratio was 1.54:1 in our patients, which was higher than the OS gender ratio in most series. One-, three-, and five-year survival rates in our patients were 87%, 61%, and 49%, respectively. Although it was not statistically significant, older age at the time of diagnosis, axial location, and male gender were the poorest prognosis factors.

## Acknowledgement

We thank all patients affected by osteosarcoma registered in the INCR between 2008, and 2014.

**Conflict of interest:** None

**Funding:** None

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