Review Article

Prognostic Factors of Hip Fracture in Elderly: A Systematic Review

Abstract

The hip fracture causes significant disabilities in many elderly people. Many studies around the world have identified various risk factors for the hip fracture. The aim of this study was to systematically investigate the risk factors of hip fractures. This study is a systematic review of risk factors for hip fractures. All published papers in English and Persian languages on patients in Iran and other countries between 2002 - 2022 were examined. The search strategy used keywords matching the mesh, including : predictors, hip fracture, and disability. Articles were selected from international databases (PubMed, Proquest ,Web of Sience, Scopus, Google scholar and Persian(Sid,Magiran), and the Newcastle Ottawa Scale was used to assess the risk of bias. The study has identified several factors that were significantly correlated with the risk of hip fracture, including age, cigarette and alcohol consumption, visual and hearing problems, low BMI levels, history of falling, weakness, and diseases such as stroke, cardiovascular disease, high blood pressure, arthritis, diabetes, dementia, Alzheimer's, Parkinson's, liver and kidney diseases, bone density, osteoporosis, vertebral fracture, and hyperthyroidism. However, the study did not find any significant correlations between the consumption of calcium and vitamin D, history of fractures, cognitive disorders, schizophrenia, and household income, and the risk of hip fracture. The results of this study reveal the determining role of some risk factors in hip fracture in older persons. Therefore, it is recommended that health policy makers provide the possibility of early intervention for some changeable factors.

Keywords: *Prognostic factors, hip Fracture, elderly, systematic review*

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Introduction

Hip fracture is one of the most common causes of fractures in older persons. The annual mortality rate of older persons with hip fractures is reported between 14% and 36%.[1] With the increase in the number of elderly and life expectancy worldwide, especially in developing countries, such as Asian, African, South American, and Middle Eastern countries, the incidence of hip fractures is also increasing,[2,3] hence it is predicted that by 2050, the number of fractures will reach 6.3 million people.[4] The high incidence of hip fractures can be related to causes such as falls, social and lifestyle changes, bone density reduction, high prevalence of drug use, low levels of calcium and vitamin D, and reduced mobility of people.[5] Hip fracture in the elderly, called "the last fracture of life," has a strong effect on their quality of life and is accompanied by an increase in social and family burdens.[6] Due to the increase in the elderly population in the world, the present study was conducted to systematically investigate the factors affecting the incidence of hip fractures.

Method

The current study was conducted based on PRISMA standards.[7]

Search strategy and information sources

The study is a systematic review of risk factors in hip fracture incidence. All the papers published in both Persian and English languages, in the patient population of Iran and other countries, and domestic and foreign journals during the period of 2002–2022 were examined. The search strategy was the keywords matching the mesh, including:

(Predictor* OR Risk Factor* OR Causality* OR Risk Score* OR Prognostic OR "Health correlate" OR "Population at risk") AND (Hip *OR *Trochanteric* OR "neck of femur" OR "lower end of femur") AND (break* OR fracture*) AND Disability* OR "Disability Evaluation" OR Frailty* OR "Frailty Syndrome" OR Debility* OR imperfection* OR weakness* OR infirmity*

Articles were selected from international databases (PubMed, Proquest, Web of Science, Scopus, Google Scholar) and Persian (Sid, Magiran). It should be noted that the OR operator was used to connect synonyms and the AND operator was used to combine the obtained results.

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Study selection and eligibility criteria

The inclusion criteria comprised cross-sectional and cohort studies, case-control studies, and clinical trials. Studies lacking necessary and related information to the topic, as well as review studies, case studies, and letters to the editor, were excluded from the study. Finally, 17 papers entered the final stage. The full texts of the articles were reviewed.

Data collection process and risk of bias assessment

The abstracts and full texts of the articles were independently checked by two researchers (KFF and SYa) and the information in the checklist included the author's name, publication year, the study location, study type, age and gender of the subjects, sample size and risk factors. Re-review was done by the first researcher to increase the accuracy and validity of the information.

The Newcastle–Ottawa Scale (NOS) was employed in this systematic review to assess the quality of articles.[8] Scores of 7–9, 4–6, and 4 were classified as having a low, moderate, or high risk of bias, respectively [Table 1].

Results

Study selection and study characteristics

In the initial review, 1295 studies were found. After removing 710 duplicate articles and 315 unrelated articles, finally, 17 articles were reviewed [Figure 1]. The characteristics of the reviewed studies (including authors, publication year, the study country, type of study, sample size, gender, age, and risk factors) are presented in Table 2.

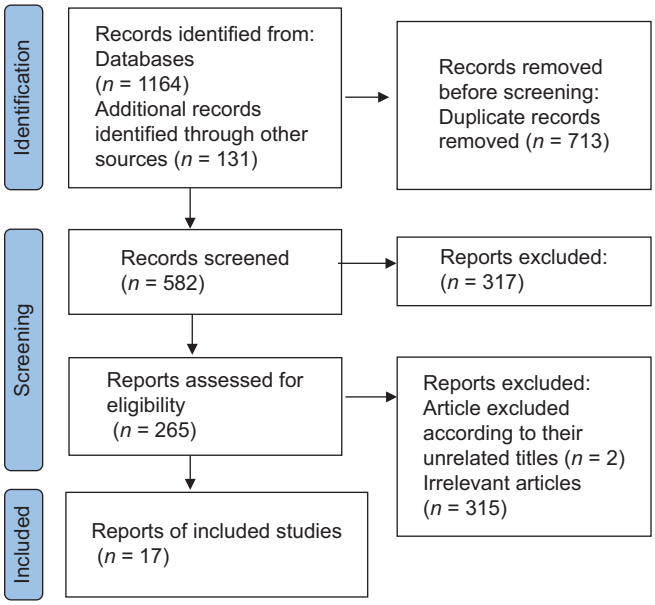

Figure 1: Flowchart of the included eligible studies in the systematic review

Results of individual studies

The results of the present study showed a significant correlation between different factors, for instance, sociodemographic factors (e.g., age, sex) lifestyle factors (e.g., cigarette and alcohol consumption), diseases (e.g., visual and hearing problems, low body mass index (BMI) levels, stroke, cardiovascular disease, high blood pressure, arthritis, diabetes, dementia, Alzheimer, Parkinson, liver and kidney diseases, bone density, osteoporosis, vertebral fracture, hyperthyroidism, hyponatremia, consume of corticosteroids), physical factors (e.g., grip strength, history of falling, weakness), social factors (e.g., death of a spouse, lack of dependence on others to move), and the risk of hip fracture. However, there was no significant correlation between the consumption of calcium and vitamin D, a history of fractures, cognitive disorders, schizophrenia, and household income, and the risk of hip fracture [Table 2].

Discussion

Gender and age

Table 2 shows that the relative risk of hip fracture in females was significantly higher than in males relative risk=(2.00 (95% CI: 1.13–3.53) and by increasing age, the risk of hip fracture increased significantly, RR = 4.17 (95% CI: 3.77–4.60). Studies have indicated that hip fractures in middle-aged and elderly women are about 90% more than in men, which can be caused by the decrease in estrogen levels in women after menopause, due to the decrease in bone density.[26,27]

Osteoporosis

The study indicates that osteoporosis had a significant relationship with the incidence of hip fracture OR= odds ratio odds ratio=1.35 (95% CI: 1.24–1.46) [Table 2]. Hip fracture is often associated with osteoporosis. A high incidence of fractures in people aged under 50 years can also be caused by osteoporosis.[28,29] Reports have shown that drug treatment of osteoporosis reduces the risk of hip fracture by 50–70%.[30,31]

Hypertension

As per this study, having high blood pressure increased the chance of hip fracture by 75% [Table 2]. The pathogenesis of osteoporosis-related fractures is based on two important

Table 1: The Newcastle Ottawa Scale for risk of bias assessment of the included studies

Study	Selection				Comparability	Outcome			Overall
Cohort	Representativeness of the exposed cohort	Selection of the non-exposed cohort	Ascertainment of exposure	Outcome (not present at the start)		Assessment of outcome	Adequacy of follow-up length	Adequacy of follow up	
Woo SH (2020)[9]	*		*	*	-/*		*	*	6
Ottenbacher KJ (2002)[10]	*	*	*	*	**	*	*	*	9
Walter LC (2003)[11]	*		*	*	-/*	*	*	*	7
Wainwright SA (2005)[12]	*	*	*	*	-/*	*	*	*	8
Alfaro-Acha A (2006)[13]	*		*	*	-/*	*	*	*	7
Nakamura K (2009)[14]	*		*	*	-/*	*	*	*	7
Barzilay JI (2013)[15]	*		*	*	-/*	*	*	*	7
Furuya T (2013)[16]	*		*	*	-/*	*	*	*	7
Sørensen HJ (2013)[18]	*	*	*	*	**	*	*		8
Lobo E, (2018)[19]	*		*	*	**	*	*	*	8
Wang HK (2014)[20]	*	*	*	*	**	*	*	*	9
Stenholm S (2015)[21]	*	*	*	*	**	*	*	*	9
Tal S (2015)[22]	*		*	*	*	*	*	*	7
Kim J (2019)[23]	*		*	*	*	*	*	*	7
Bhandari SK (2020)[24]	*	*	*	*	**	*	*	*	9
Vala CH (2020)[25]	*	*	*		**	*	*	*	8
Clinical trial	**Selection**				**Comparability**	**Exposure**			**Overall**
	Is the case definition adequate?	**Representativeness of the cases**	**Selection of controls**	**Definition of controls**		**Ascertainment of exposure**	**Same method of ascertainment for cases and controls**	**Non-response rate**	
Pekkarinen T (2013)[17]	*	*	*	*	**	*	*		8

Table 2: Studies reporting risk factors of hip fracture

ID	Author (years of publication)	Geographical area of the study	Type of study	Age	Sample size (male and female)	Sample size (male)	Sample size (female)	Case	Control	Risk factor
1	Woo SH (2020)[9]	Korea	Retrospectively	>60	507	173	334			Sex
										Age ≥75
										Osteoporosis medication
										Hypertension
										Diabetes mellitus
										Myocardial infarction
										Cerebrovascular accidents
										Liver disease
										Chronic kidney disease
2	Ottenbacher KJ (2002)[10]	Mexican American	Prospective cohort	>65	2884	1213	1671			Insulin diabetes
										Age
										Sex (female)
										Ever smoker
										BMI
										Stroke
										Diabetes mellitus
										Age
										Sex (female)
										Ever smoker
										BMI
										Stroke
3	Walter LC (2003[11]	USA	Prospective cohort study	55–104	5187					Age ≥75
					2548					Ethnicity (white)
					366					Transferring (independent or partially dependent)
					5187					Age ≥75
					718					Asian
					624					Latino
					2548					White
					3678					Sex (female)
					1555					Living situation (Home alone)
					987					Living situation (group alone)
					449					Toileting (dependent)
					366					Transferring (independent or partially dependent)
					526					Walking (dependent)
4	Wainwright SA (2005)[12]	USA	Cohort	≥65			6667			Age (without osteoporosis)
							6667			Walking for exercise
							6667			Other activity: Alone or in addition to walking
							6667			Contrast sensitivity, low frequency
							6667			Any falls in last year
							6667			Prevalent vertebral fracture
							6667			Total hip bone mineral density (per SD decrease)
							1398			Previous hyperthyroidism (with osteoporosis)
							1398			Distance depth perception: Lowest quartile

Contd...

Table 2: Contd...

ID	Author (years of publication)	Geographical area of the study	Type of study	Age	Sample size (male and female)	Sample size (male)	Sample size (female)	Case	Control	Risk factor
							1398			Contrast sensitivity, low frequency
							1398			Grip strength (per 5 kg)
							1398			Prevalent vertebral fracture
							1398			Total hip bone mineral density (per SD decrease)
5	Alfaro-Acha A (2006)[13]	USA	Prospective cohort	≥65	2653	1117	1531			BMI
										Age
										Sex (female)
										Unmarried
										Current smoker
										Vision scale
										Short physical performance battery
										Medical conditions (heart attack, stroke, diabetes, and arthritis)
6	Nakamura K (2009)[14]	Japan	Cohort study	<80–≥90	7654	1565	4085			Dementia
					7654					Total score of the Barthel index
					3579					Special nursing homes
					4085					Sex (female)
					2664					Age group (80–89)
					1322					≥90
					490					Vision (partially or blind)
					859					Hearing (having partial or total hearing loss)
					1338					Levels of dementia (light)
					1643					Levels of dementia (moderate)
					684					Levels of dementia (severe)
					2400					Calcium supplementation
					481					Past history of upper or lower limb fractures
					183					Past history of other fractures
7	Barzilay JI (2013)[15]	USA	Cohort	≥65		1276				Albuminuria
							1834			Albuminuria
8	Furuya T (2013)[16]	Japan	Cohort	42–69	9720		7980			Sex (female)
										Age
										BMI
										DAS28
										J-HAQ score (total)
										J-HAQ score (arising)
										J-HAQ score (hygiene)
										J-HAQ score (eating)
										J-HAQ score (activity)
										J-HAQ score (walking)
										J-HAQ score (dressing)
										J-HAQ score (reaching)
										J-HAQ score (gripping)
										Patient pain VAS
										Physician global VAS
										CRP 0.3–1.0 vs ≤0.3 mg. 100 Ml
										CRP >1.0 vs ≤0.3 mg. 100 ml
										History of any prior fracture

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Table 2: Contd...

ID	Author (years of publication)	Geographical area of the study	Type of study	Age	Sample size (male and female)	Sample size (male)	Sample size (female)	Case	Control	Risk factor
										History of TKR
										Daily prednisolone dose, mg 1 day
										Bisphosphonate use
										Active vitamin D3 use
										Proton pump inhibitor use
										Biologic use
										Weekly MTX dos
										Folic acid use
										Duration of RA 2–10 years vs <2 years
										Duration of RA >10 years vs <2 years
										RF positive (>20 IU/mL)
9	Pekkarinen T (2013)[17]	Finland	Controlled trial	60–70			2178			Smoking
										Age
										Fall history
										Stroke history
					15431					Schizophrenia diagnosis
10	Sørensen HJ (2013)[18]	Denmark	Cohort	NA	3353771					Sex (male)
										Age
										Early retirement pension
										Somatic score ≥1
										Antipsychotic
										Corticosteroids
										Lifetime alcohol abuse
										Antidepressants
										Anticholinergics
										Benzodiazepines
11	Lobo E (2018)[19]	Spanish	Longitudinal	>55	4660	1976				Mini-mental Status Examination (MMSE) in men
										MMSE Staging (questionable)
										Mild
										Moderate
										Severe
										Petersen's mild cognitive impairment (MCI-P)
								2684		MMSE in women
										MMSE staging (questionable)
										mild
										Moderate
										Severe
										Petersen's mild cognitive impairment (MCI-P)
										DSM-5 mild neurocognitive disorder
12	Wang HK (2014)[20]	Taiwan	Retrospective, cohort	≥60	1408					Dementia
					183					Alzheimer
					1225					Unspecific dementia
					1059					Dementia non-osteoporosis group
					349					Dementia osteoporosis group

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Table 2: Contd...

ID	Author (years of publication)	Geographical area of the study	Type of study	Age	Sample size (male and female)	Sample size (male)	Sample size (female)	Case	Control	Risk factor
13	Stenholm S (2015)[21]	Swedish	Prospective cohort	16–65		11232				Being on sick leave for >3 months
						2375				Being on sick leave (1–15 days)
						26109				Being on sick leave (16–75 days)
						14276				Being on sick leave (166–365 days)
							13078			Being on sick leave for >3 months
							29984			Being on sick leave (1–15 days)
							33347			Being on sick leave (16–75 days)
							14514			Being on sick leave (166–365 days)
14	Tal S (2015)[22]	Israel	Retrospective study	>65	1161	303	858			Sex (female)
										Frailty
										Fall
										Diabetes mellitus
										Parkinson's disease
										Normal calcium
										Normal albumin
										Normal hemoglobin
15	Kim J (2019)[23]	South Korea	Retrospective cohort	≥65	90012					Sex (women)
										Age 70–74
										75–79
										80–84
										>85
										Type of health security
										Household income (low)
										Household income (middle)
										Severity of disability (severe)
										Severity of disability (mild)
										Charlson comorbidity index (1–2)
										Charlson comorbidity index+3
										Stroke
										Parkinson
										Osteoporosis
16	Bhandari SK (2020)[24]	USA	Retrospective cohort	≥55						Hyponatraemia
										Sub-acute hyponatraemia
										Chronic hyponatraemia
17	Vala CH (2020)[25]	Swedish	Retrospective cohort	60–100			128344			Month 0–6 in men After death of a spouse compared with still-married men
										Month 6–12
										Year 2
										Year 3
										Year 4
						299067				Over 5 years
										Month 0–6 in women after the death of a spouse compared with still-married men
										Month 6–12
										Year 2
										Year 3
										Year 4
										Over 5 years

Contd...

Table 2: Contd...

ID	OR	HR (adjusted)	HR (unadjusted)	RR (relative risks; adjusted)	RR (unadjusted)	Incidence rate ratio (IRR)
1	1.92 (0.91–4.02)					
	1.16 (0.61–2.21)					
	0.55 (0.20–1.46)					
	1.75 (0.92–3.31)					
	1.44 (0.69–3.01)					
	1.57 (0.50–4.88)					
	1.48 (0.54–4.08)					
	1.20 (0.26–5.50)					
	1.38 (0.44–4.37)					
2		2.84 (1.49–5.43)				
		1.06 (1.03–1.09)				
		1.7 (1.07–2.72)				
		1.12 (0.73–1.73)				
		0.95 (0.91–0.99)				
		1.49 (0.65–3.42)				
		1.57 (1.03–2.39)				
		1.06 (1.03–1.09)				
		1.86 (1.21–2.88)				
		1.03 (0.69–1.54)				
		0.96 (0.92–1.00)				
		1.21 (0.56–2.61)				
3		2.00 (1.40–2.80)				
		2.10 (1.60–2.80)				
		3.00 (1.20–7.20)				
			2.30 (1.60–3.20)			
			1.30 (0.80–2.20)			
			1.50 (0.90–2.70)			
			2.50 (1.70–3.80)			
			1.50 (1.10–2.00)			
			1.50 (1.10–2.20)			
			2.70 (1.90–3.90)			
			1.70 (1.00–3.20)			
			3.10 (1.30–7.60)			
			2.30 (1.20–4.30)			
4		1.08 (1.05–1.12)				
		0.73 (0.48–1.09)				
		0.50 (0.32–0.78)				
		1.54 (1.06–2.25)				
		1.64 (1.15–2.34)				
		1.86 (1.28–2.71)				
		1.95 (1.53–2.46)				
		1.86 (1.11–3.10)				
		1.67 (1.11–2.53)				
		1.56 (1.03–2.37)				
		0.74 (0.59–0.94)				
		1.52 (1.00–2.29)				
		1.52 (1.09–2.10)				
5		0.98 (0.94–1.03)				
		1.03 (0.99–1.07)				
		1.45 (0.85–2.49)				
		0.90 (0.55–1.47)				
		0.81 (0.49–1.34)				

Contd...

Table 2: Contd...

ID	OR	HR (adjusted)	HR (unadjusted)	RR (relative risks; adjusted)	RR (unadjusted)	Incidence rate ratio (IRR)
		1.08 (0.74–1.59)				
		0.94 (0.87–1.02)				
		1.30 (1.00–1.68)				
6				1.87 (1.12–3.12)		
				2.66 (1.57–4.53)		
					1.76 (1.10–2.82)	
					2.00 (1.13–3.53)	
					2.00 (1.16–3.46)	
					1.80 (0.95–3.38)	
					0.91 (0.42–1.98)	
					1.16 (0.67–2.02)	
					2.50 (1.41–4.42)	
					1.96 (1.10–3.50)	
					1.92 (0.93–3.65)	
					1.37 (0.91–2.60)	
					1.66 (0.90–3.04)	
					0.70 (0.17–2.83)	
7		1.02 (0.89–1.17)	1.13 (1.02–1.27)			
		1.12 (1.00–1.25)	1.15 (1.05–1.25)			
8		0.74 (0.40–1.35)	1.01 (0.58–1.76)			
		1.56 (1.26–1.91)	1.87 (1.53–2.28)			
		0.91 (0.85–0.97)	0.92 (0.86–0.99)			
		0.84 (0.64–1.10)	1.33 (1.14–1.56)			
			2.99 (2.37–3.77)			
		1.74 (1.28–2.36)	2.40 (1.99–2.88)			
		1.58 (1.11–2.24)	2.63 (2.11–3.29)			
		1.18 (0.83–1.67)	2.05 (1.70–2.47)			
		1.14 (0.80–1.63)	2.22 (1.84–2.67)			
		1.03 (0.74–1.42)	2.36 (1.94–2.88)			
		0.96 (0.68–1.36)	2.23 (1.82–2.72)			
		0.84 (0.59–1.20)	1.95 (1.62–2.34)			
		0.87 (0.62–1.23)	1.89 (1.62–2.34)			
		1.01 (0.99–1.01)	1.02 (1.01–1.02)			
		1.00 (0.99–1.02)	1.01 (1.00–1.03)			
		1.46 (0.86–2.47)	1.93 (1.17–3.19)			
		1.03 (0.57–1.88)	1.84 (1.11–3.04)			
		1.34 (0.86–2.10)	1.61 (1.04–2.50)			
		3.28 (1.37–7.83)	7.34 (3.17–16.96)			
		1.01 (0.96–1.07)	1.04 (1.01–1.06)			
		1.07 (0.65–1.77)	2.01 (1.25–3.23)			
		1.38 (0.85–2.24)	2.31 (1.44–3.69)			
			1.40 (0.72–2.69)			
			0.68 (0.17–2.77)			
			1.02 (0.98–1.07)			
			1.11 (0.70–1.76)			
			1.11 (0.36–3.43)			
			2.16 (0.72–6.53)			
			1.32 (0.81–2.14)			
9	4.32 (2.14–8.71)					
	1.15 (1.03–1.28)					
	2.27 (1.24–5.90)					

Contd...

Table 2: Contd...

ID	OR	HR (adjusted)	HR (unadjusted)	RR (relative risks; adjusted)	RR (unadjusted)	Incidence rate ratio (IRR)
	2.99 (1.19–7.54)					
						1.00 (0.90–1.11)
10						0.73 (0.71–0.74)
						1.08 (1.08–1.08)
						2.33 (2.26–2.39)
						1.09 (1.07–1.11)
						1.19 (1.15–1.24)
						1.44 (1.36–1.53)
						2.80 (2.72–2.87)
						1.18 (1.16–1.12)
						1.29 (1.22–1.36)
						1.06 (1.04–1.08)
11		0.93 (0.89–0.97)				
		1.88 (0.56–6.28)				
		4.99 (1.39–17.91)				
		2.51 (0.39–16.43)				
		9.31 (1.35–64.06)				
		0.61 (0.15–2.56)				
		0.98 (0.95–1.01)				
		0.88 (0.52–1.48)				
		1.37 (0.79–2.40)				
		1.03 (0.50–2.12)				
		2.81 (0.91–8.62)				
		1.19 (0.72–1.98)				
		1.10 (0.60–2.02)				
12		1.92 (1.48–2.49)	2.03 (1.63–2.52)			
		2.19 (1.43–1.87)	2.31 (1.57–2.76)			
		1.87 (1.33–2.83)	2.01 (1.49–2.93)			
		1.84 (1.37–2.46)	2.04 (1.59–2.62)			
		2.27 (1.28–4.01)	1.98 (1.24–4.01)			
13		1.96 (1.74–2.20)				
		1.40 (1.27–1.56)				
		1.21 (1.13–1.31)				
		1.31 (1.22–1.14)				
		1.55 (1.41–1.70)				
14	1.39 (1.05–1.82)					
	1.36 (1.06–1.75)					
	1.49 (1.16–1.90)					
	1.33 (1.02–1.72)					
	0.60 (0.41–0.87)					
	0.68 (0.52–0.89)					
	1.27 (0.92–1.74)					
	0.70 (0.55–0.89)					
15	1.49 (1.39–1.61)					
	1.67 (1.52–1.83)					
	3.04 (2.77–3.32)					
	4.17 (3.77–4.60)					
	4.09 (3.62–4.62)					
	0.52 (0.45–0.59)					

Contd...

Table 2: Contd...

ID	OR	HR (adjusted)	HR (unadjusted)	RR (relative risks; adjusted)	RR (unadjusted)	Incidence rate ratio (IRR)
	1.00 (0.92–1.09)					
	0.98 (0.91–1.06)					
	1.59 (1.33–1.89)					
	1.68 (1.49–1.88)					
	1.10 (1.02–1.18)					
	1.24 (1.03–1.49)					
	1.27 (1.13–1.43)					
	1.51 (1.04–2.19)					
	1.35 (1.24–1.46)					
16		1.30 (1.22–1.39)				
		1.52 (1.42–1.62)				
		1.00 (0.92–1.08)				
17		1.84 (1.68–2.03)				
		1.60 (1.47–1.74)				
		1.54 (1.44–1.64)				
		1.50 (1.40–1.61)				
		1.38 (1.27–1.50)				
		1.33 (1.28–1.38)				
		1.62 (1.53–1.71)				
		1.51 (1.43–1.60)				
		1.47 (1.41–1.54)				
		1.38 (1.32–1.45)				
		1.36 (1.30–1.42)				
		1.38 (1.34–1.42)				

OR (95%CI)=odds ratios (OR) and 95% confidence intervals (95% CI), HR (95%CI)=hazard ratio (HR) and 95% confidence intervals (95% CI), RR (95%CI)=relative risk (RR) and 95% confidence intervals (95% CI), IRR (95%CI)=incidence rate ratio (IRR) and 95% confidence intervals (95% CI)

factors, including bone density and falls, both of which are potentially influenced by high blood pressure. In addition, blood pressure predicts hip fractures in women more than men.[32] However, blood pressure patients who are treated with thiazides have fewer fractures due to higher bone density.[33]

Diabetes mellitus and insulin diabetes

Diabetes mellitus increases the risk of hip fracture by 57% [Table 2]. The adverse effects of diabetes on the skeletal structure and increasing the risk of osteoporosis, the reduction of cartilage tissue and mineral salts, and finally, the incidence of fracture have been reported in many studies.[34-36] A meta-analysis study found that in patients with hip fractures, the risk of developing pressure sore showed a significant increase.[37] On the other hand, diabetes due to complications, such as neuropathy, retinopathy, cognitive impairment, muscle weakness, and hypoglycemic events caused by the use of antidiabetic drugs, puts a person at risk of falling.[38] In this study, insulin use significantly increased the risk of hip fracture HR = 2.84 (95% CI: 1.49–5.43) [Table 2]. Long-term use of insulin with anabolic effects on bone tissue plays an important role in increasing the risk of fracture.[35,39]

Myocardial infarction

The chance of hip fracture in patients with myocardial infarction was reported to be 57 times more than others [Table 2]. One of the most important causes of death in hip fracture patients or those who undergo hip fracture surgery is cardiovascular diseases, especially myocardial infarction.[40,41] Some genetic factors, such as oxidative stress, which significantly increases in the elderly with hip fractures, may be the determining factor in the relationship between bone mass reduction, fracture, and cardiovascular diseases.[42,43]

Cerebrovascular accidents and stroke

The mechanism of stroke in hip fracture patients is somewhat unknown although factors, such as physical immobility, mental stress, and post-fracture pain, play a significant role in its occurrence.[44] Embolism in the brain through internal or external shunts of the heart, as well as the systemic hypercoagulative state after surgery for femur fracture, is effective in causing stroke.[45,46] On the other hand, hospitalization and surgery of hip fracture patients with physiological changes during anesthesia make the person susceptible to cerebrovascular accidents.[44] In a study, the mortality rate in hip fracture patients with a history of stroke was higher than other patients who did not have a history

of stroke,[47] which can be the reason for the importance and clinical attention to prevent falls in these patients.[48] In the present study, the findings show a 2.99 times greater chance of hip fracture in patients with a stroke [Table 2].

Liver disease

According to the findings, the chance of hip fracture in liver patients is 1.2 times higher than in others [Table 2]. Studies have indicated that the risk of osteoporosis and hip fracture increases in patients with liver diseases.[49,50] In addition, the low level of insulin-like growth factor 1 (IGF-1) in patients with advanced liver cirrhosis may destroy the regeneration and preservation of bone mass in elderly patients and cause fractures.[49] Liver disorders are often associated with the risk of venous thromboembolism, hypo and hypercoagulopathy, infection, hemodynamic instability, and malnutrition. On the other hand, a disorder in bone tissue metabolism is associated with a decrease in recovery and a delay in the patient's mobility, and all of these factors may cause the patient's death.[51]

Chronic kidney disease and albuminuria

In the current study, kidney diseases increased the chance of hip fracture by 38% [Table 2]. The increased risk of hip fracture in patients with kidney diseases may be related to mineral, bone, and weakness disorders.[52] In addition, the decrease in kidney function is associated with the disorder of the parathyroid–calcium–phosphate axis.[53] It is worth mentioning that calcium and phosphate are the main mineral components of bone. In addition, hyperphosphatemia has a positive relationship with the occurrence of fractures in patients with chronic kidney diseases.[54] A decrease in bone density due to hyperphosphatemia can be due to the increase of osteoblasts through IGF-1 and the osteopontin gene.[55] Parathyroid hormone changes bone cell proliferation, especially osteoblasts and osteoclasts, which may affect calcium absorption and bone metabolism.[56] In addition, the increase in albumin levels in kidney disorders is directly related to the occurrence of osteoporosis and fractures. Aging of the musculoskeletal system causes the loss of muscle mass and physical strength, which plays a crucial role in creating the risk of fractures.[15]

Smoking

Smoking showed a significant relationship with the risk of hip fracture, OR = 4.32 (95% CI: 2.14–8.71) [Table 2]. Smoking disrupts calcium absorption and vitamin D metabolism and reduces bone density by reducing the level of 25-hydroxy vitamin D.[56] Smoking usually causes people to lose weight by reducing their appetite and increasing the free radicals level, causing bone decay and eventually fracture.[57] In addition, the reduction in the consumption of vitamins E and C in smokers and the toxic effect of nicotine in cigarettes reduce blood supply to bones and increases the risk of hip fracture.[58,59]

Alcohol

In this study, lifelong alcohol consumption was associated with a significant increase in the incidence of hip fracture [Table 2]. Studies have indicated that excessive or moderate alcohol consumption in the elderly can be associated with the risk of fractures. It is worth mentioning that the effect of alcohol on the occurrence of fractures varies depending on the amount of bone damage. Excessive consumption of alcohol by reducing bone density or by changing endocrine signals and having a negative effect on bone regeneration plays an important role in the occurrence of fractures.[60,61]

BMI

Low weight along with weakness, chronic inflammation, and reduced physical health increases the risk of falling and fractures. Underweight increases the risk of hip fracture by reducing bone mineral density (BMD). On the other hand, obesity has a protective effect on fractures by increasing the BMD and reducing the impact of falls due to the soft tissue layer.[62,63] According to the findings, BMI has a protective effect on hip fracture [Table 2].

Ethnicity

Ethnicity through genetic factors and factors, such as smoking, nutrition, physical activity, and mineral concentration, play an important role in osteoporosis and fractures.[64] Studies have shown a high rate of hip fracture in European and American countries, but Latin American, African, and Asian countries have the lowest rate.[65,66] In this study, the risk of hip fracture was significantly observed in white people more than in others [Table 2].

Transferring

The risk of hip fracture in those who were able to move without the help of others was significantly higher than in those who were dependent on others for moving HR = 3.0 (95% CI: 1.2–7.2) [Table 2]. Studies have shown that the elderly who are dependent on others for moving are less prone to fractures. On the other hand, a person's dependence on others is associated with a decrease in quality of life, a decrease in mobility, and an increase in bedsores.[11] The risk of fracture in people who are able to move causes a conflict between important goals such as maintaining the individual's independence and preventing fracture.[67]

Living situation

Living alone in the elderly significantly increased the risk of hip fracture HR = 1.5 (95% CI: 1.1–2.2) [Table 2]. Studies have shown that the survival rate in patients with hip fractures is higher in people who live alone.[68,69] The link between social relationships with better functioning of the immune system and the reduction of inflammatory processes over time can have a positive effect in all parts

of life. Social support can have an important effect named 'buffering effect' on stress during hip fracture.[69,70]

Walking

In this study, walking played a protective role against hip fracture [Table 2]. Epidemiological studies have shown that the risk of hip fracture decreases by increasing physical activity. Activities, such as cleaning, gardening, walking, and cycling, have an inverse relationship with hip fractures in the elderly.[71,72] In a prospective study, elderly women who did housework for more than 9 hours had 22% fewer hip fractures compared to those who did 5 hours a day.[73]

Fall and vertebral fracture

Falling significantly increased the chance of hip fracture OR = 2.27 (95% CI: 1.24–5.90) [Table 2]. According to studies, more than 90% of hip fractures in the elderly occur due to falls.[74,75] Falling on the side causes a severe blow to the trochanter, which causes excessive pressure on the superolateral cortex of the femur, where the bone structure has a thin cortex due to old age and is inherently fragile.[76,77]

In the present study, the risk of hip fracture was 86% higher in those with vertebral fractures than others [Table 2]. In a study, the results showed that a quarter of the people who were referred with hip fractures had asymptomatic vertebral fractures at the same time.[78] The results of studies have shown that the risk of hip fracture in women whose vertebrae are deformed is 3.4 times higher than in other women. Therefore, the radiologist's clinical evaluation of vertebral fractures can be effective in identifying women who are at risk of hip and spine fractures.[79] Vertebral fractures along with hip fractures are often due to osteoporosis and low bone quality.[78]

BMD

BMD is the main determinant of the risk of fractures caused by osteoporosis.[80] BMD decreases in people aged over 50 years so the amount of BMD reduction in the femoral neck is 0.64% before the age of 65 and 0.36% after the age of 65.[81] By decreasing one standard deviation in BMD, the risk of hip fracture increases 2.6 times.[82] In the current study, the risk of hip fracture was significantly related to BMD (HR = 1.95 (95% CI: 1.53–2.46) [Table 2].

Hyperthyroidism

Hyperthyroidism was associated with an 86% increase in the risk of hip fracture [Table 2]. Hyperthyroidism in adults is one of the causes of secondary osteoporosis and ultimately fractures. On the other hand, excessive treatment with levothyroxine and thyroid stimulating hormone (TSH) suppressive therapy plays an important role in reducing BMD and finally fractures.[83] In subclinical hyperthyroidism, the TSH serum level in the presence of free triiodothyronine (T3) and free thyroxine (T4) is at the lowest normal level, which can be associated with a decrease in bone health and affect the occurrence of fractures.[84,85]

Grip strength

Evaluating handgrip strength (HGS) is a general measure of body strength and physical performance. HGS has been reported as one of the important functional outcomes in hip fracture patients.[86,87] The decrease in muscle strength reduces the mechanical load of the body's skeleton and is associated with a decrease in bone regeneration. Moreover, the loss of muscle mass leads to impaired neuromuscular function and a decrease in mechanical load and ultimately increases the risk of falls and fractures.[88] According to the findings of the present study, the risk of hip fracture showed a significant relationship with HGS [Table 2].

After the death of a spouse and single

Being single had a protective effect against hip fracture, while the death of a spouse increased the risk of fracture by 62% [Table 2]. Reports have indicated that women who have lost their spouses are mostly suffering from one or more chronic diseases, such as high blood pressure, diabetes, heart disease, stroke, and reduced physical activity and stress, caused by the death of their spouses and their conditions have worsened compared to before.[25] It can also lead to an unhealthy diet and more use of cigarettes and alcohol, which is effective in increasing the risk of hip fracture and can be seen years after the death of the spouse. On the other hand, the findings of studies have shown the relationship between being single and death after hip fracture due to the lack of social support.[70,89] Increased death and decreased survival after hip fractures have also been seen in young men who live alone.[70]

Vision

Poor vision is very common in the elderly. Diseases, such as cataracts, glaucoma, and macular degeneration, are all strongly age-related. Poor vision or differences in visual acuity between eyes, as well as reduced contrast sensitivity, were associated with an increased risk of fracture,[90] which is consistent with the findings of the present study regarding the relationship between visual impairment and the risk of hip fracture [Table 2].

Hearing

According to the present study, hearing increases the risk of hip fracture by 16% [Table 2]. The pathophysiological relationship between hip fracture and chronic otitis media can be due to inflammation and genetic factors. Inflammation plays a role in the pathogenesis of hearing and osteoporosis. Osteoporosis is associated with a decrease in bone mass as well as in bone density of the cochlea and a disturbance in sound transmission to the cochlea, which ultimately leads to hearing loss.[91] Therefore, it seems necessary to examine the middle ear in patients with

osteoporosis. In addition, the relationship between hearing loss and falls and eventually fractures has been proven in studies.[92]

Dementia

The prevalence of dementia increases with age. In Alzheimer's disease with mild, moderate, and severe spectrum, hip fracture has been reported to be relatively constant.[93] In patients with dementia and hip fracture, some risk factors are the same such as weight loss, low vitamin D levels, decreased digestive absorption of calcium, and increased parathyroid hormone levels. Decreasing the level of vitamin D and calcium is effective in reducing bone density and plays an important role in hip fracture.[94] In the present study, dementia significantly increased the risk of hip fracture [Table 2].

Psychopathology and Pharmacological Treatment

No significant relationship was found between the incidence of hip fracture and schizophrenia. However, there was a significant relationship between antipsychotics, antidepressants, anticholinergics, corticosteroids, and benzodiazepines with the incidence of hip fracture [Table 2]. The occurrence of fractures in schizophrenia patients can be due to the effects of psychoactive drugs and low quality of life. On the other hand, the side effects of some antipsychotics, antidepressants, and benzodiazepines such as sedation, drowsiness, and orthostatic hypotension affect people's balance and walking, leading to falls and ultimately fractures.[95] In addition, the femoral head is vulnerable to corticosteroids due to the stress of weight bearing and reverse blood flow. Also, corticosteroids with hypertrophy of fat cells can cause venous occlusion, vessel occlusion, compression of small veins, and increase the pressure inside the bone, resulting in blood stasis, ischemia, and bone death.[96]

Parkinson's disease

Parkinson's disease is associated with low levels of bone density, vitamin D deficiency, osteoporosis, and fractures.[97] On the other hand, falls in patients with Parkinson's disease are associated with reduced functional ability and finally death. Studies have shown that prevention with vitamin D and bisphosphonates can be effective in reducing the risk of non-vertebral fractures in patients with Parkinson's disease.[98,99] In this study, Parkinson's disease significantly increased the chance of hip fracture by 51% [Table 2].

Arthritis

In the present study, a history of arthritis significantly increased the risk of hip fracture [Table 2]. Chronic inflammation, use of glucocorticoids, and lack of physical activity cause bone tissue loss in patients with rheumatoid arthritis (RA) and the risk of osteoporosis increases. The release of pro-inflammatory cytokines, such as interleukin 1 (IL-1), IL-6, and tumor necrosis factor-α, causes the abnormal production of osteoclasts and the balance between absorption and bone formation is disturbed. Moreover, immobility caused by inflammation, muscle pain, weakness, and swelling caused by RA may increase the risk of falling to some extent and thus increase the rate of bone fracture.[100]

Hyponatraemia

Studies have indicated that hyponatraemia significantly increases the risk of hip fracture. HR = 1.30 (95% CI: 1.22–1.39) [Table 2]. Hyponatraemia is usually asymptomatic or manifests with symptoms such as walking disorder, falling, or impaired bone fracture healing.[101] It can also play an effective role in reducing cellular immunity by disrupting the function of IL-17 and the production of T helper cells. On the other hand, it can accelerate the aging process by causing osteopenia, hypogonadism, sarcopenia, cardiomyopathy and reducing body fat. These factors also increase the risk of death by increasing weakness in the elderly.[102]

Calcium and vitamin D3

According to the findings of the present study, the consumption of calcium and vitamin D3 had no significant relationship with the occurrence of hip fracture [Table 2]. Vitamin D is necessary for optimal skeletal-muscular health with calcium absorption, mineralization, formation of osteoid tissue in bones, and maintenance of muscle function. The low status of vitamin D causes secondary hyperparathyroidism, bone loss, and muscle weakness. On the other hand, consuming high doses of vitamin D by producing toxic effects in the body can be associated with an increase in the risk of falls and fractures.[103] In addition, the results of meta-analysis studies have indicated the fact that the consumption of vitamin D alone is not effective in reducing the risk of hip fracture in the elderly.[104]

Past history of upper or lower limb fractures and other fractures

According to studies, having a history of fracture can predict the risk of fracture due to osteoporosis and hip fracture in shorter periods.[105,106] About 25% of patients with a history of fracture experience subsequent fractures, since the risk level of the next fracture is cumulative and the risk level does not return to the level before the fracture.[107] In this study, there was no significant relationship between the history of fracture and the risk of hip fracture [Table 2].

Cognitive impairment and frailty: Being on sick leave for more than 3 months

Maintaining cognitive function with factors, such as aging, trauma, and multiple diseases, can be a sign of brain resilience. Being physically fit, mastering several languages, and having a higher education level can lead to brain resilience. On the other hand, these factors play an important role in predicting cognitive improvement after

hip fracture.[108] In this study, no significant relationship was found between cognitive disorders and the risk of hip fracture, while long-term absence from work and weakness increased the risk of hip fracture by 96% and 36%, respectively [Table 2]. Long-term absence indicates a person's lack of health, and suffering from some chronic diseases, reduced immunity, and low quality of life increase the risk of falling and eventually fractures.[21] Therefore, information related to the long-term absence of people can be very effective in identifying high-risk groups of hip fractures.

Weakness is a state of vulnerability caused by a decrease in the ability to maintain or restore homeostasis in the face of stressful factors.[109] In most studies, weakness is a predictor of outcomes such as mortality,[110] incidence of complications,[111] length of hospitalization,[112] quality of life, and discharge.[113] Studies have mentioned the relationship between weakness and the risk of hip fracture.

Household income

The results indicated that the income level of the family had no significant relationship with the incidence of hip fracture [Table 2], while some studies have mentioned the relationship between the low level of income and the incidence of hip fracture. The low levels of income, education, and physical activity in leisure time can be effective in the occurrence of fractures.[114,115] However, the increase in income level is also associated with eating habits that may lead to the occurrence of osteoporosis and ultimately fractures.[116]

Death of a spouse

The study results showed a significant increase in the risk of hip fracture in overweight men who lost their spouses [Table 2]. Stressful events in life are associated with a decrease in hip bone density and an increase in falls and fractures.[25] Loneliness can increase the risk of hip fracture by 85%. Mourning also increases the risk of death in people, although the risk of death decreases with time.[117]

Conclusion

The results of this study reveal the determining role of some risk factors including sociodemographic factors, lifestyle factors, diseases, physical factors, and social factors on hip fractures among the elderly. Therefore, it is recommended that health policymakers provide the possibility of early intervention for some changeable factors.

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Conflicts of interest

There are no conflicts of interest.

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