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Burden of Osteoporosis in Iran

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Abstract

Osteoporosis is the most common metabolic bone disease. In addition to morbidity, osteoporotic fractures also increase mortality risk in affected patients. Enough evidence is not available to indicate that, like western countries, osteoporosis is a public health problem in Iran. Therefore EMRC planned to estimate the burden of osteoporotic fractures in year 2001 based on existing sources of data. The EMRC study on bone density, the MOH study on unintentional injuries, and international literature on mortality risk following osteoporotic fractures were the main sources of information used for this study. To estimate burden of osteoporotic fractures, the prevalence of osteoporosis, the incidence of osteoporotic fractures, and the relative risk of mortality following these fractures were approximated. The mean duration of disability following major osteoporotic fractures was estimated through epidemiologic modeling. Assumptions on the disability weights of morbid conditions resulting from osteoporotic fractures were made through comparing these conditions with similar ones in Global Burden of Disease Study. Based on mortality and incidence rates, mean durations of disability, and disability weights; the DALYs indicator was calculated for Spine, Hip, and Forearm fractures. In women hip, spine, and forearm fractures were responsible for 15880, 1269, and 121 mortality- and morbidity-related lost years of life respectively. Similar figures in men were 16495, 2225, and 37 years. Collectively osteoporosis deprived Iranian population from 36026 healthy years of life (18757 in men and 17270 in women) in 2001. Higher burden of osteoporosis in men, mainly results from higher risk of mortality following fractures in male sex. The national study on unintentional injuries indicates that the incidence of osteoporotic hip fractures in Iranian population is much less than other populations. Higher bone mineral density and other probable differences between Iranians and other populations that affect fracture risk, like environmental conditions and life style, should be investigated as probable determinants of this difference. Limited available sources of information regarding osteoporotic fractures necessitate more comprehensive studies to clarify all aspects of this health problem.

Keywords: *Burden of osteoporosis, DALY, Fracture, Mortality, Iran.*

Introduction

The population health is the final outcome of a complex set of interacting factors that continuously affect individuals' health. Undertaking actions to improve population health equitably is one of the major state responsibilities (1). Considering resource constraints, through continuous monitoring of population health, states should recognize major community health needs and try to reduce their burden using efficient interventions (2).

Osteoporosis is the most common metabolic bone disease that is characterized by low bone mass and abnormal bone structure. This disease is preventable and treatable, but since it is silent until the first fracture, a small number of patients are diagnosed and managed in an appropriate time. In most cases, even after the first fracture, an effective treatment is not provided to reduce the risk of following fractures (3). Compared to general population, mortality risk is higher in patient suffering from osteoporosis-

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related fractures (4). Following hip fracture, both short and long term mortality risks are increased (5). Although otherwise anticipated, mortality risk is also increased following vertebral fractures (6). The quality of life decreases in the majority of fracture patients as a result of progressive pain and discomfort (7-9). Many hip fracture patients remain hospitalized for a considerable period and do not return back to their pre-fracture health state after discharge (4).

In western countries osteoporosis is a public health problem (1) and has absorbed significant amount of resources for research and publicity. This has attracted everyone's attention to osteoporosis even in those countries where enough evidence is not available to bring this condition to the level of a public health problem. The purpose of this study was to use existing sources of information to check whether osteoporosis has changed to a public health problem in Iran or not. Burden of disease approach, developed by WHO, is adopted for this purpose. Since the Ministry of Health is busy conducting the first National Burden of Disease Study (10), it will be possible to recognize the relative importance of osteoporosis among other diseases in near future.

Until the last decade of the previous century, a systematic and consistent effort had not been practiced to calculate burden of diseases based on "lost years of life" approach. In this decade, Harvard School of Public Health in collaboration with World Health Organization and World Bank developed DALYs

(Disability Adjusted Life Years) as the burden indicator and, based on it, calculated the Global Burden of Disease for the first time. DALYs is composed of two components. The first component, YLL (Years of Life Lost), shows the years of life lost due to premature death and the second component, YLD (Years Lived with Disability), captures the years lost to disability. Numbers of deaths by cause and standard life expectancy for different ages are all that we need for calculating the first component. To calculate YLD we need to know the number of incident cases of non-fatal outcomes and the mean duration of each one of them.

DALYs = YLL + YLD

DALYs is a normative indicator with many values included in it. The value of the time spent with non-fatal outcomes, standard life expectancy, age weighting, and discount rate are the value concerns of DALYs. Therefore the following information is required for calculation of DALYs (11).

1. Population by age and sex
2. General mortality rate by age and sex
3. Cause-specific mortality rate by age and sex
4. Non-fatal outcome incidence by age and sex
5. Mean duration of non-fatal outcomes
6. Disability weight of non-fatal outcomes
7. Standard life table
8. Age weights
9. Discount rate

All indicators required for calculation of DALYs are neither available nor, when available, are internally consistent. To operationalize burden of disease calculation, epidemiologic models were used in Global Burden of Disease Study to build a set of internally consistent indicators based on existing information (12).

Materials and Methods

Burden of osteoporosis results from the burden of fractures attributable to reduced bone density. A fracture is considered osteoporosis-related if it is either associated with reduced bone density or its incidence increases with age. Based on these criteria spine, rib, hip, arm, forearm, and clavicular fractures are considered to be osteoporosis-related in older age groups. Among these the spine, hip, and forearm are the most common sites of osteoporosis-related fractures (7). Therefore it proved justifiable to sum up the burden of these three common fractures in over 50 age group, to estimate the burden of osteoporosis in Iran in 2001.

Source of Information

The following studies were used to estimate the burden of osteoporosis:

1. The EMRC study on the prevalence of osteoporosis in Tehran, Tabriz and Mash-had (13)
2. The Ministry of Health study on the incidence of unintentional injuries in 9 provinces. In this study in a 4.5 month period all accidents that had led to hospitalization were registered.Among registered accidents fractures caused by falls from same level or low altitude in over 50 individuals were considered to be osteoporosis-related (14).
3. Literature on the mortality following osteoporotic fractures (4-6).

The Steps of Estimating the Burden of Osteoporosis

1. Determining the prevalence of osteo- porosis in Iran: EMRC study on bone mineral density was the source of data for determining the prevalence of osteoporosis in Iran. A random sample of 20 to 70 year old individuals were tested in Tehran, Mash-had, and Tabriz (1200 samples per city) in this study. BMD was determined using DXA method. Osteoporosis was defined as T score≤-2.5 in femoral neck region. Since a significant number of osteoporotic fractures occur in over 70, we had to estimate the prevalence of osteoporosis in this age group also. The prevalence of osteoporosis increases exponentially with age (15). In order to estimate the prevalence of osteoporosis in over 70 an exponential curve was fit to known age-specific prevalence points, considering their 95% confidence intervals. Based on this curve, the prevalence of osteoporosis was extrapolated to over 70 age group.

2. Determining the incidence rates of osteoporotic fractures: The study of the Ministry of Health on the incidence of unintentional injuries was used to estimate the incidence of osteoporotic fractures (14). In this study the characteristics of all accidents that had led to hospitalization in 9 provinces covering a population of about 9 million (9262527) were registered using 260 interviewers and 10 different types of questionnaires. The patient, his/her relatives, health personnel, and medical records were used as the sources of information. The study covered a 4.5 month period from July to November 2003. All hospitals in the study provinces were participating in injuries registration. The falls questionnaire was used to estimate osteoporotic fractures incidence rates. Patient's demographic information, the time and the place of fall, the height, the victim's activity when fall happened, and the injuries resulting from the fall were recorded in the questionnaire. In order to use the fall questionnaire for estimating osteoporotic fractures incidence rates, it was assumed that all spine, forearm, pelvic, and femoral fractures that had occurred in over 50 individuals were osteoporosis-related. In the questionnaire two types of injuries under the names of pelvic and femoral fractures were found and femoral neck or pelvic fractures were not used to denote any type of injury. Considering that femoral neck fracture is the most common fall-related fracture in older age groups, it seems that most of injuries recorded under the names of pelvic or femoral fractures in over 50 victims can be assumed to be femoral neck fracture. To avoid under-numeration of hip fractures, it was decided to regard all injuries recorded under the names of pelvic or femoral fractures as hip fracture. We had not access to the raw data of the MOH study and the incidence rates of fall-related injuries in over 50 individuals were the only information that we succeeded to receive. The population information published in the Statistical Yearbook of Iran Statistical Center had been used to calculate incidence rates. Since the gathered data was covering a 135 day period, the numbers of registered fractures had been multiplied by 2.7 to approximate yearly numbers. Age distribution of fracture rates was required for DALYs calculation. Assuming that the age distribution of fracture rates is proportional to the

age distribution of osteoporosis prevalence, the total incidence rate of fractures in 50+ individuals was broken down among 50-59, 60-69, and 70+ age groups.

3. Determining mortality rates following fractures: Mortality risk increases and remains higher than age-matched general population mortality rate for several years following hip and vertebral fractures (4). These findings mean that these fractures could not be considered as short-term events to let the injured patient to return back to normal daily life after completion of the treatment period, but the victim has to suffer from the complications of the accident till the end of his/her life. Therefore the remission rate was assumed to be zero in hip and vertebral fractures. In forearm fracture the patient usually completely recovers after a 3 month period. Forearm fracture is not associated with increased mortality in men, but women experience a higher mortality risk following this fracture. The relative risks of mortality following forearm, hip, and vertebral fractures were estimated based on the study conducted by Johnell et al. on Swedish patients (4). In this study 2847 fracture patients were followed for 5 years and relative risks of mortality by sex and the year after the fracture have been measured in 60-79 and 80+ age groups (Fig. 1). Based on these measurements the mortality risk decreases almost linearly following hip and vertebral fractures and increases linearly in general population. These lines intersect after a few years and the mortality risk in fracture patients equals the risk in general population. For example, the risk of mortality following hip fracture in 80+ age group equals the risk in general population after 11 years in men and 8 years in women. A single value for the relative risk of mortality was calculated through dividing the overall mortality rate of patients in years that they are exposed to a higher risk of mortality by the mortality in general population.

4. Estimation of indicators required for calculation of DALYs: Epidemiologic modeling has been used in Global Burden of Disease Study for estimating required indicators. WHO has especially designed the DisMod software for this purpose (12). In addition to demographic information, the software needs three indicators from the following list as inputs of the model.

- Incidence rate
- Prevalence
- Disease-specific mortality rate
- Case fatality rate or relative risk of mortality
- Remission rate
- Mean duration of the disease

All six indicators are calculated as the output of the model while they are internally consistent. In this study incidence rate of osteoporotic fracture, relative risk of mortality in fracture patients, and remission rate were used as model inputs. From model outputs incidence rate, mortality rate, and duration were used for DALYs calculation.

5. Value concerns: The weight of a disability is the lost proportion of the time spent with it. There are a number of well-developed techniques for determining disability weights (16). The weights used for similar disabilities in Global Burden of Disease Study were adopted for this study (17). The disability weights adopted for hip, spine, and forearm fractures are 0.247, 0.05, and 0.18 respectively. To make the results of this study comparable with other burden of disease studies, all values regarding standard life table, discount rate, and age weighting adopted in Global Burden of Disease Study were also used in this study (11).

6. Calculating DALYs: YLL and YLD of fractures were calculated using the template designed for this purpose by WHO (17). Demographic information, discount rate and age weighting are required for calculating both YLL and YLD. Mortality rate and standard life table are the specific inputs for YLL calculation. Incidence, duration, and disability weight are the information specifically required for

calculating YLD. DALYs is the algebraic sum of YLL and YLD.

Results

Prevalence of osteoporosis by age and sex is shown in Table 1. Table 2 included incidence rates of osteoporosis-related fractures. According to this table, hip fracture is the most common hospitalized fracture in both sexes. Vertebral fracture is less frequent than hip and forearm fractures in both sexes. Relative risks of mortality following osteoporotic fractures are shown in Table 3. Using DisMod outputs (Table 4) and disability weights, the burden of hip, spine, and forearm fractures were calculated in Iranian population in 2001 (Table 5). Total years of life lost were found to be 15880 years for hip fracture, 1269 years for vertebral fracture, and 121 years for forearm fracture. Collectively osteoporosis was found to be responsible for 36027 years of life lost due to premature mortality and disability (18757 years in men and 17270 years in women). (Fig. 2)

Table 1: Estimated prevalence of osteoporosis by age and sex in Iran (per 10000)

Age group (year)	Men	Women
20-29	13	13
30-39	30	40
40-49	66	119
50-59	147	358
60-69	328	1077
70+	729	3234
Total	104	318

Table 2: Incidence of major osteoporotic fractures by age and sex in Iran (per 100000)

Age group (year)	Spine		Hip		Forearm	
	Men	Women	Men	Women	Men	Women
50-59	6.9	3.1	38.1	33.1	12.2	13.2
60-69	15.3	9.5	84.8	99.4	27.2	39.6
70+	34.1	28.4	188.7	298.6	60.5	118.9

Table 3: Relative risk of mortality following osteoporotic fractures

Age group (year)	Spine		Hip		Forearm	
	Men	Women	Men	Women	Men	Women
50-59	8.4	8.1	5.3	7.2	1.0	2.5
60-69	6.7	6.3	4.6	5.7	1.0	2.0
70+	5.1	4.5	3.9	4.2	1.0	1.5

Table 4: DisMod outputs regarding prevalence, incidence, mortality and duration of major osteoporotic fractures based on Iran population in year 2001

Site of fracture	Sex	Prevalence per 10^3 (Numbers)	Incidence per 10^3 (Numbers)	Mortality per 10^3 (Numbers)	Mean duration-years
Spine	Women	0.07 (2081)	0.01 (416)	0.01 (220)	6.36
	Men	0.07 (216)	0.02 (540)	0.01 (352)	4.7
Hip	Women	0.69 (21982)	0.14 (4337)	0.07 (2191)	6.56
	Men	0.59 (19541)	0.11 (3633)	0.07 (2213)	6.09
Forearm	Women	0.01 (432)	0.06 (1807)	0.00 (13)	0.25
	Men	0.01 (283)	0.04 (1171)	0.00 (0)	0.25
Total	Both sexes	(46390)	(11904)	(4989)	

Table 5: DALYs by fracture site and sex

	YLL		YLD		DALYs		DALYs	DALYs per 1000		DALYs per 1000
	Men	Women	Men	Women	Men	Women	Both sexes	Men	Women	Both sexes
Hip	12814	11532	3681	4318	16495	15880	32375	0.5	0.5	0.5
Spine	2135	1188	89	81	2225	1269	3493	0.1	0.1	0.1
Forearm	0	69	37	53	37	12.1	158	0	0	0
Total	14949	12789	3807	4482	18757	17270	36026	0.57	0.54	0.56

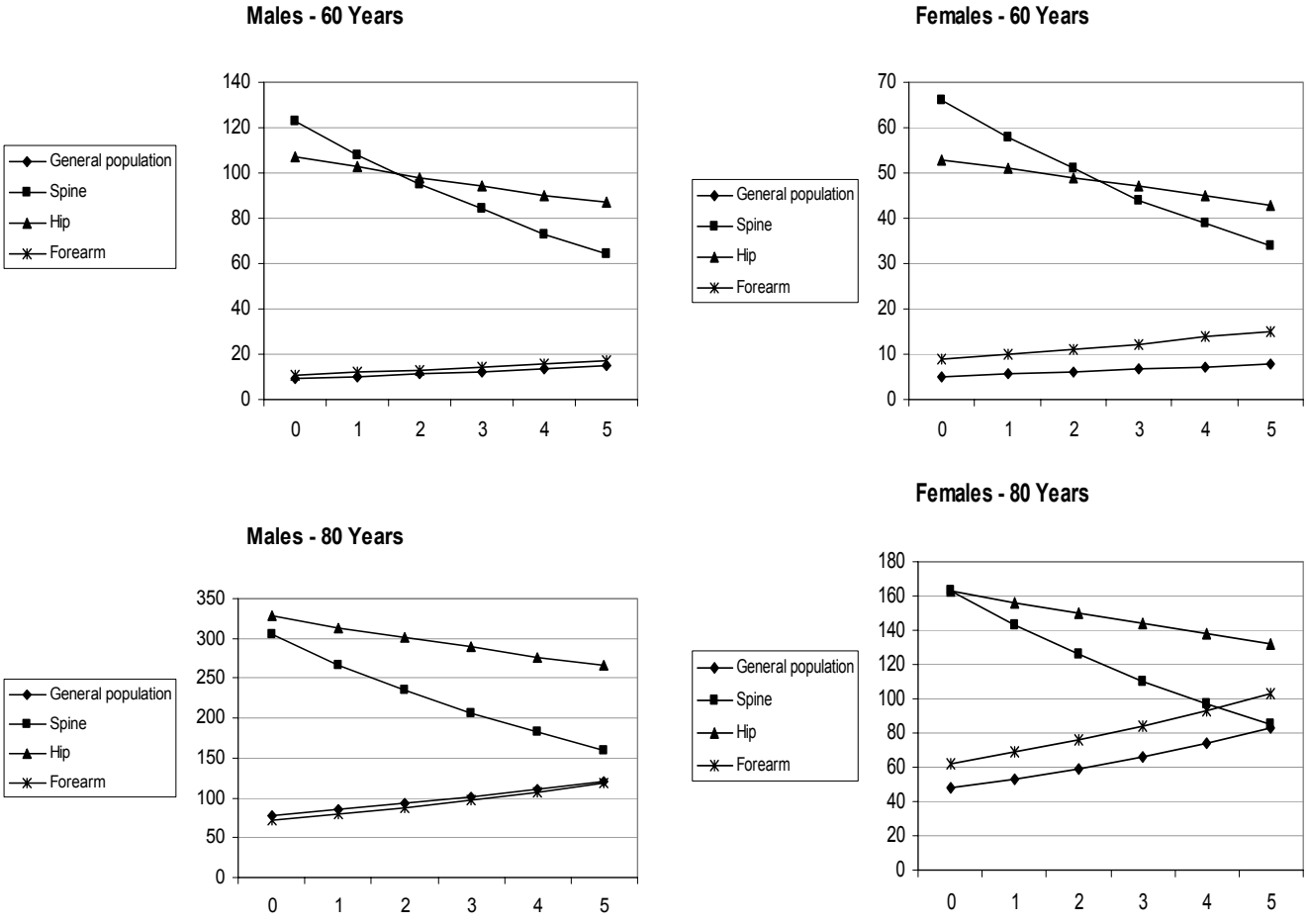

Fig. 1: Mortality risk following osteoporotic fractures by age and sex. These charts are based on the data presented in the following paper. Johnell O. et al. Mortality after Osteoporotic Fractures, Osteoporosis Int. (2004) 15:38-42

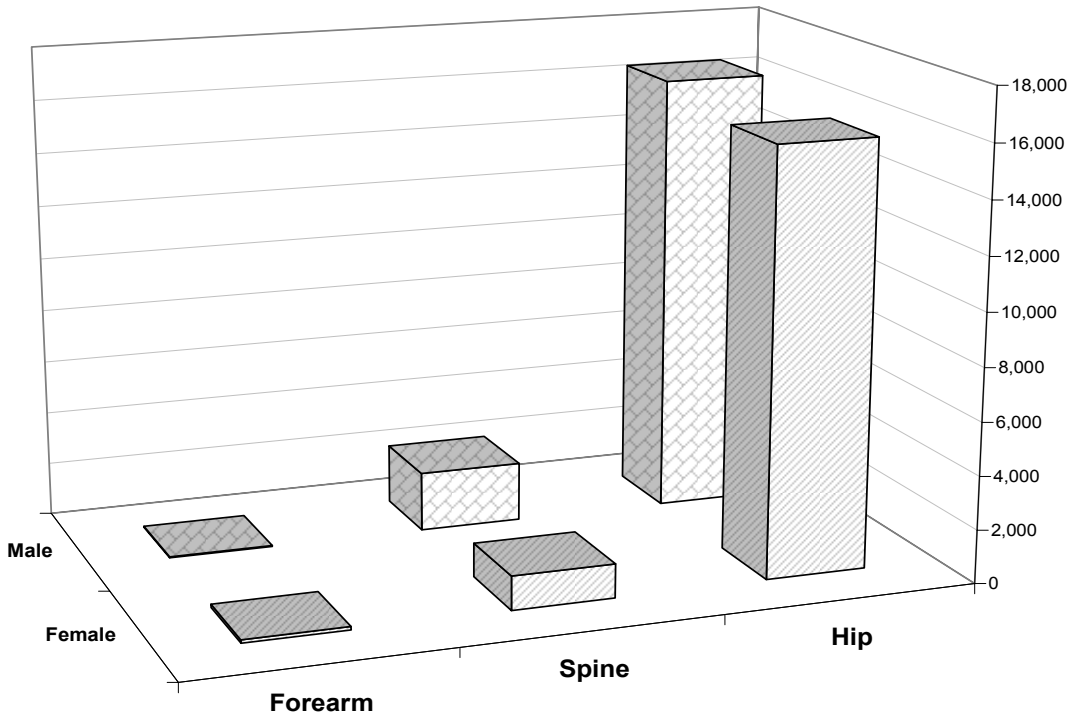

Fig. 2: Burden of major osteoporotic fractures by sex in Iran in 2001

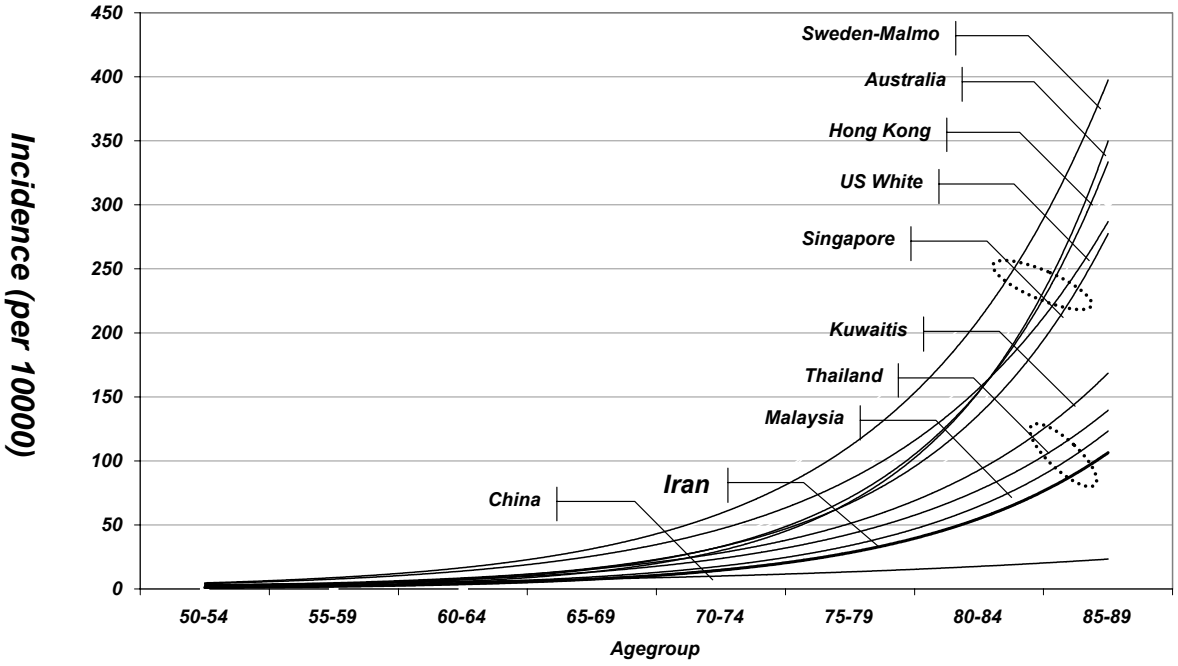

Fig. 3: Comparison of female hip fracture in different countries

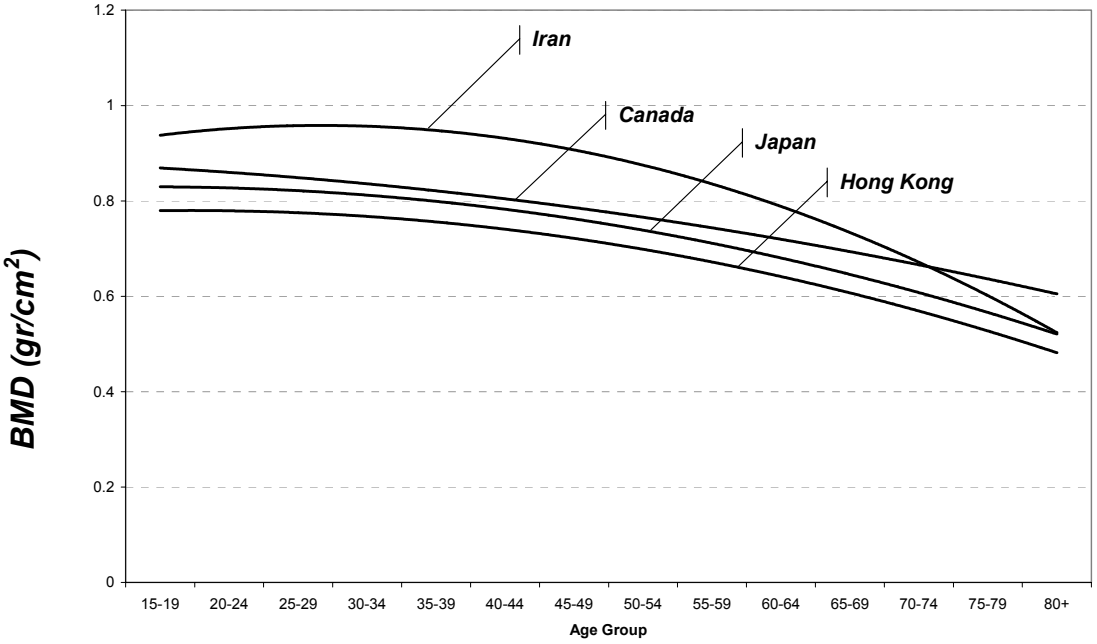

Fig. 4: Comparison of femoral neck BMD by age among Iranian, Japanese, Hong Kongian, and Canadian women

Discussion

The values obtained for the burden of osteoporosis-related fractures do not solely convey any messages unless compared with burdens of other diseases at the same period or the burden of same fractures in other periods. Since the results of the National Burden of Disease Study being conducted by the MOH, has not yet been published (18); it is not possible to compare osteoporosis with other diseases at national level, but this will be possible in near future. Osteoporosis was not included in Global Burden of Disease Study. Therefore it is not possible to compare the burden of osteoporosis in Iran with its burden in other countries and regions. Estimating the burden of osteoporosis for the first time in Iran makes it impossible to analyze its trend across time. Therefore the interpretation of the number that we have obtained for the burden of osteoporosis in Iran should be postponed until availability of similar numbers in other places or times.

Despite higher prevalence of osteoporosis and osteoporotic fractures in women, the burden of osteoporosis was higher in men in this study. This unexpected result could be attributed to:

1. Most vertebral fractures remain either undiagnosed or are not hospitalized for management. Therefore vertebral fracture is subject to under-numeration in this study and available numbers do not reflect its real magnitude and sex distribution.
2. Men are exposed to a higher mortality risk after hip fracture. Therefore despite higher incidence of hip fracture in women, more years are lost in men due to premature death.

As shown in Fig 3, the incidence of hip fracture in Iranian women is much less than what are reported from other countries (7, 19-25). To explain this difference, first of all the bone mineral density (BMD) of Iranian women should also be compared with other countries. Based on the EMRC study, we had access to the BMD of Iranian women living in Tehran, Tabriz, and Mash-had. Comparison of values obtained from this study with the BMD of Japanese (26), Hong Kongian (27), and Canadian (28) women clearly shows that the bone

density is higher in Iranian women (Fig. 4). Therefore lower incidence of hip fracture in Iranian women maybe attributable to higher BMD. Considering that BMD is not the only determinant of hip fracture and also the limited sources of information for estimating fracture incidence and comparing BMD, more precise conclusions about the real risk of osteoporotic fractures in Iranian older age groups should be based on more comprehensive studies.

Registration of hospitalized unintentional injuries was the major source of information in this study. Therefore the limitations of this study mainly stem from the limitations of the registration that its primary focus was not to capture osteoporotic fractures. Most vertebral fractures and many forearm fractures are managed as outpatients and the values obtained for their incidence based on registered data do not represent their real occurrence at community level.

It is not practical to manage hip fracture cases as outpatients. Therefore given that all fracture cases have access to hospital beds and all hospitals are included in registration, the number of admitted hip fractures could be considered as the real number of hip fracture events. Based on the registration protocol the second condition is met. The results of the National Utilization Survey (18) could be used to check whether hospital beds are accessible or not. According to the results to this study the success rate in 50-64 year old individuals who attempted to receive an ambulatory care was found to be 97.8%. This rate for attempted hospitalization was 90%. Similar success rates for 65+ individuals were 97.4% and 94%. Therefore the validity of obtained values for hip fracture incidence rate could be considered acceptable.

Generalizability is another concern when attempting to use registered data as country estimates. South-eastern, eastern and northern parts of the country are not represented in injuries registration. Therefore registered data should cautiously be used for assessing the osteoporotic fracture risk in the whole country.

Estimating age distribution of fracture incidence in over 50 individuals should also be considered as a limitation. This limitation stems from 1) extrapolating osteoporosis prevalence in lower age groups to obtain the prevalence in 70+ age group using an exponential curve and 2) estimating age distribution of fracture incidence solely based on age distribution of osteoporosis prevalence. Neither extrapolation is a completely valid way to estimate unknown values nor is the BMD the sole predictor of fractures. Therefore the real age distribution of fracture incidence rates may be different from what we have estimated.

Since quality of care the patient receives following fracture affects his/her survival, using Swedish risks of mortality should be considered another limitation of this study. Lack of similar studies on Iranian patients made this limitation unavoidable.

All limitations of this study stem from limitation in sources of data. Since having a not very clear picture is always preferred to lacking any ones, trying to estimate the burden of a disease solely based on limited sources of data is at all times justifiable. In depth understanding of data gaps and the quality of existing sources of data is the most important achievement of the first round of the burden of disease study. Based on such an experience and in order to obtain a clearer picture of the burden of osteoporosis in Iran, it is recommended to register injuries in more representative regions of the country with special focus on osteoporotic fractures and to follow fracture patients for a better understanding of their quality of life and survival.

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