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Osteoporosis screening for patients with prolonged use of glucocorticoid in national guard hospital – Jeddah, Saudi Arabia

Abstract

Background: Glucocorticoid therapy is the most common secondary cause leading to osteoporosis. Bone mineral density testing is recommended for those who are going to use steroids for more than three or six months. However, many patients are on prolonged steroid therapy and have never been screened for osteoporosis.

Objective: The aim of this study was to assess if patients with prolonged use of steroids are checked for osteoporosis in National Guard Hospital, Jeddah, Saudi Arabia.

Methods: This cross-sectional study was carried out on male and female patients on 5mg of prednisolone for more than 6months in National Guard Hospital, Jeddah, Saudi Arabia. Data were extracted from patients' files and included patients' demographics; dose and duration of prednisolone use; screening for osteoporosis and medication taken to treat or prevent osteoporosis.

Results: Files of 362 patients were included. Most patients were women (82.6%) and had prednisolone dose ≥5mg daily for more than 6months (78.5%). Those diagnosed with osteoporosis constituted 21%. Dual energy x-ray absorptiometry (DEXA) scan was done in 40.9% of patients, irrespective of the dose or duration of use of prednisolone. The majority of patients were given calcium and vitamin D (93.9% and 84.5%, respectively); while only 27.1% had bisphosphonate. Increase in age was associated with a decreased risk (patients were more likely to have DEXA scan); while patients with increased body mass index (BMI) were more likely not to have DEXA scan, compared to the underweight.

Conclusion: the rates of DEXA Scan performance were suboptimal. Treatment received by the patients on chronic steroid medications is satisfactory to a large extent. However, doctors' awareness should be raised as regards patients at high risk of developing glucocorticoid induced osteoporosis (GIOP) and the appropriate use of bisphosphonates. We recommend developing National Saudi Guidelines for management of GIOP, and it should be distributed to all health care facilities that manage those patients.

Keywords: glucocorticoids, osteoporosis, DEXA scan, calcium, vitamin D, bisphosphonates

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Introduction

Osteoporosis is a disease characterized by a decrease in the density of normally mineralized bones and an increased risk of fragility fractures.[1] It is a worldwide problem especially in developed countries, where it represents the most prevalent metabolic bone disease.[2] Osteoporosis can affect both males and females. It has been estimated that about one-half of all postmenopausal women and one-quarter of white men over 60years of age will sustain a fracture as a result of osteoporosis in their lifetime.[3] In Saudi Arabia, 34% of women and 30.7% of men aged 50-79years suffer from osteoporosis.[4]

Osteoporosis is usually asymptomatic and manifests as fractures of hip, vertebra, or other bones. The gold standard diagnostic method is dual energy x-ray absorptiometry (DEXA) scan, and the diagnosis is made when the bone density is equal or less than 2.5 standard deviation below that of a young adult.[5] However, most individuals with osteoporosis remain undiagnosed and untreated. It has been reported that despite an expected prevalence of about 25% among women over 60years, less than 2% of them were diagnosed as having osteoporosis by their primary care physicians, and only one-third of diagnosed patients were given the proper drug therapy.[6] The problem of misdiagnosis and under-treatment is even worse in men with osteoporosis.[7] Several risk factors contribute to osteoporosis, and they are classified into primary and secondary factors. Primary risk factors, such as increasing age and female gender, are the most common among all factors. Secondary risk factors are potentially modifiable and include chronic glucocorticoid use, hyperthyroidism, hyperparathyroidism, alcohol abuse, vitamin D deficiency, and immobilization. Among all secondary causes, glucocorticoid-induced osteoporosis (GIOP) is the most common secondary cause leading to osteoporosis.[1] Glucocorticoids are considered the mainstay treatment of variety of diseases. However, the risk of GIOP is significantly associated with the duration and dose of glucocorticoid use. It is estimated that the overall risk of GIOP after 6months of steroid use is 50%, while fracture risk after fiveyears of its use is 30%.[8,9] Regarding the dose, glucocorticoids at doses as low as prednisone 3mg are associated with fractures.[10]

The mechanism of GIOP is unknown, however some theories suggest that steroids have an inhibitory effect on osteoblasts. In addition, it is suggested that steroids decrease intestinal absorption of calcium and increase its renal excretion.[11] Due to the high risk of

fracture and related disabilities caused by GIOP, multiple guidelines have been released about the screening of osteoporosis for patients on steroid treatment or planned to start glucocorticoid therapy. For example, the American College of Rheumatology recommends bone mineral density (BMD) testing for patients planned to use steroids for more than sixmonths, while Osteoporosis Society of Canada recommends BMD testing for all patients having more than 2.5mg/day prednisone for more than 3months.[12] However, many patients are on prolonged steroid therapy and have never been screened for osteoporosis. So, the aim of this study was to assess if patients with prolonged use of steroids are checked for osteoporosis in the National Guard Hospital, Jeddah, Saudi Arabia.

Methods

Ethical considerations:

The study got an ethical approval from the Institutional Review Board of King Abdullah International Medical Research Center, Jeddah, Saudi Arabia. Confidentiality of the collected data and participant's privacy were assured, and the data were used only for research purpose. The study did not have any physical, psychological, social, legal, economic, or any other anticipated risks to participants, and it did not present a direct benefit for the study's participants.

Study design

A descriptive, cross-sectional design was adopted.

Participant's eligibility criteria

The target population of this study was male and female patients on 5mg of prednisolone or more daily for 6months or more in the National Guard Hospital, Jeddah, Saudi Arabia. Patients diagnosed with hyperparathyroidism, those on prednisolone less than 5mg, 5mg for less than 6months and patients using prednisolone for less than one month were excluded from the study.

Sample size and sampling technique

According to Ledwich and Clarke,[13] the percentage of patients on corticosteroid who were checked for osteoporosis were 37%. Hence, to reach our aim, we needed to recruit 352 participants to be 95% confident with 5% margin of error. We used a consecutive sampling technique to include patients' files meeting the inclusion criteria until the calculated sample size is met.

Setting and dates

The study was conducted in the National Guard Hospital, Jeddah, Saudi Arabia. Data collection was done during the period from 1st of April, 2019 to 31st of May, 2019.

Data collection instrument

The data were collected from patients' files, and included patients' demographics (age, gender, BMI); the dose and duration of prednisolone use; screening for osteoporosis (including vitamin D and calcium blood levels, thyroid function tests, and DEXA scan); and preventive or treatment measures for osteoporosis.

Data entry and statistical analysis

Data analysis was carried out using SPSS version 22. All numerical variables were checked for normality by Shapiro-Wilk test. Normally distributed variables were expressed as means ± standard deviation, and differences between groups were tested by Student's unpaired T test. Categorical variables were summarized as frequencies and percentages, and association between variables was tested using Pearson's Chi square or Fisher-Freeman-Halton Exact Tests as appropriate. Binary logistic regression analysis was carried out to identify factors that affect screening with DEXA Scan. A p-value of <0.05 was considered statistically significant.

Results

The files of 362 patients were included. Figure 1 illustrates that the study sample consisted mostly of women (82.6%); the most frequently prescribed prednisolone dose ≥5mg daily (78.5%); and those diagnosed with osteoporosis constituted 21%.

Table 1 summarizes the sociodemographic data of the studied patients. The age of the studied sample ranged from 15 to 86years old; with a mean age 49.1±15. Evaluation of the BMI revealed that 30.1% were obese; 24.6% were overweight; and 19.6% were extremely obese. The duration of prednisolone use was above 12 to 24months in most cases (72.3%). Patients were categorized into two groups according to the prednisolone dose (those administering ≥5mg daily for more than 3months and 7mg or more daily for more than 1 month). There was no significant difference in the age between the two groups (p=0.294). Also, there was no significant association between dose and gender (p=0.385) or BMI (p=0.065). A significantly higher frequency of patients on the >7mg dose administered prednisolone for either 3-6months (16.7%), or >24months (48.7%); while a significantly higher frequency of patients on the ≥5mg dose have taken treatment for >12-24months (78.9%) (Figure 2). Study of the patients diagnosed with osteoporosis showed that they had higher mean age (62.6±12.4 vs 45.5±14.3); while no significant association existed with gender (p=0.676), BMI (p=0.389), dose of prednisolone (p=0.289), or duration (p=0.227).

Table 2 shows the screening tests done for diagnosis of osteoporosis, as well as the received prophylaxis/treatment. The most frequently performed tests included levels of: albumin (99.2%), alkaline phosphatase (98.6%), vitamin D (95%), and creatinine (93.6%). The least performed test was calcium level (1.1%). DEXA Scan was done in 40.9% only of patients. The prophylaxis/treatment received in the majority of cases was calcium (93.9%) and vitamin D (84.5%); Bisphosphonate was administered in 27.1% of cases only. There was no significant association between the dose of prednisolone and any of the screening tests (except for parathormone level that was performed more in those taking >7mg); and the prophylaxis/treatment (except for calcium that was administered more frequently in those taking ≥5mg). As regards gender, there was no significant association with any of the tests done (except for DEXA Scan that was performed more frequently in women). A significantly higher frequency of men administered bisphosphonate. The number of patients who did not receive any treatment was 6 (1.7% of total cases); half of them were diagnosed with osteoporosis. Most patients had two drugs (65.2%), 21% had three drugs, and 12.2% had only one drug; with no significant difference between the two prednisolone doses. A significantly higher percentage of women had three drugs (23.4% vs 9.5%; p=0.045). Figure 3 illustrates the duration of use of prednisolone and having DEXA Scan or medications. There was no significant association (p>0.05).

Table 3 demonstrates the screening tests and the received prophylaxis/treatment in men above 70years and women above

65years-who are at high risk of developing osteoporosis. In all cases, levels of alkaline phosphatase, and albumin were performed. The frequency of performing screening tests was generally higher than the total sample. The most commonly used prophylaxis/treatment was vitamin D in men above 70years and calcium in women above 65years. Also, bisphosphonate was administered by more women than men. All the three men had two drugs; while 7% of women had no drugs at all. Table 4 defined the characteristics of patients at risk of not having DEXA Scan, while being on long term steroid therapy. Only age and BMI had a significant effect. Increase in age was associated with a decreased risk (patients were more likely to have DEXA Scan); while patients with increased BMI were more likely to not have the investigation, compared to the underweight.

Table 1 Sociodemographic data of the studied patients

		Total (n=362)		Dose				Osteoporosis			
				≥5mg daily (n=284)		7mg daily (n=78)		Yes (n=76)		No (n=286)	
Age	Min-Max	15	86	15	84	21	86	25	84	15	86
	Mean±SD	49.1	15.6	48.7	16.2	50.5	13.2	62.6	12.4	45.5	14.3
	p			0.294				<0.001*			
Gender	Male	63	17.40%	52	18.30%	11	14.10%	12	15.80%	51	17.80%
	Female	299	82.60%	232	81.70%	67	85.90%	64	84.20%	235	82.20%
	p			0.385				0.676			
BMI	Underweight	15	4.10%	13	4.60%	2	2.60%	4	5.30%	11	3.80%
	Normal	78	21.50%	62	21.80%	16	20.50%	15	19.70%	63	22.00%
	Overweight	89	24.60%	63	22.20%	26	33.30%	14	18.40%	75	26.20%
	Obese	109	30.10%	94	33.10%	15	19.20%	29	38.20%	80	28.00%
	Extremely obese	71	19.60%	52	18.30%	19	24.40%	14	18.40%	57	19.90%
	p			0.065				0.389			
Dose of prednisolone	≥ 5mg daily for ≥ 6 months	284	78.50%					63	82.90%	221	77.30%
	7mg daily	78	21.50%					13	17.10%	65	22.70%
	p							0.289			
Duration	≤3months	13	3.50%	0	0.00%	13	16.7	0	0.00%	14	4.90%
	3-6months	12	3.30%	0	0.00%	12	15.4	2	2.60%	11	3.80%
	>6-12months	60	16.60%	48	16.90%	12	15.4	11	14.50%	49	17.10%
	>12-24 months	262	72.30%	224	78.90%	38	48.7	61	80.30%	199	69.60%
	>24months	15	4.10%	12	4.20%	3	3.8	2	2.60%	13	4.50%
	p			<0.001*				0.227			

*significant at p<0.05.

Citation: Al-Aidarous S, Al-Husayni F, Alzahrani J, et al. Osteoporosis screening for patients with prolonged use of glucocorticoid in national guard hospital – Jeddah, Saudi Arabia. *Endocrinol Metab Int J.* 2019;7(4):113–120. DOI: 10.15406/emij.2019.07.00254

Table 2 Screening for osteoporosis and treatment in the studied groups

		Total		Osteoporosis		Dose				Gender			
				Yes (n=76)		≥5mg daily (n=284)		7mg daily (n=78)		Male (n=63)		Female (n=299)	
		n	%	n	%	n	%	n	%	n	%	n	%
Screening test													
Vitamin D level	Done	344	95.00%	75	98.70%	272	95.80%	72	92.30%	57	90.50%	287	96.00%
	p					0.239				0.102			
Calcium Level	Done	4	1.10%	0	0.00%	3	1.10%	1	1.30%	0	0.00%	4	1.30%
	p					1				1			
ALP level	Done	357	98.60%	76	100.00%	279	98.20%	78	100.00%	62	98.40%	295	98.70%
	p					0.589				1			
Phosphate level	Done	344	95.00%	76	100.00%	272	95.80%	72	92.30%	59	93.70%	285	95.30%
	p					0.239				0.531			
Magnesium level	Done	200	55.20%	35	46.10%	152	53.50%	48	61.50%	33	52.40%	167	55.90%
	p					0.207				0.614			
Albumin Level	Done	359	99.20%	76	100.00%	281	98.90%	78	100.00%	62	98.40%	297	99.30%
	p					1				0.437			
Creatinine level	Done	339	93.60%	75	98.70%	266	93.70%	73	93.60%	59	93.70%	280	93.60%
	p					1				1			
PTH level	Done	111	30.70%	25	32.90%	79	27.80%	32	41.00%	13	20.60%	98	32.80%
	p					0.025*				0.058			
TSH level	Done	315	87.00%	69	90.80%	247	87.00%	68	87.20%	47	74.60%	268	89.60%
	p					0.961				0.001*			
DEXA Scan	Done	148	40.90%	65	85.50%	109	38.40%	39	50.00%	17	27.00%	131	43.80%
	p					0.064				0.014*			
Prophylaxis/treatment													
Calcium	Yes	340	93.90%	69	90.80%	272	95.80%	68	87.20%	57	90.50%	283	94.60%
	p					0.012*				0.242			
Vitamin D	Yes	306	84.50%	60	78.90%	242	85.20%	64	82.10%	55	87.30%	251	83.90%
	p					0.494				0.503			
Bisphosphonate	Yes	98	27.10%	47	61.80%	74	26.10%	24	30.80%	55	87.30%	209	69.90%
	p					0.407				0.005*			
Number of drugs	None	6	1.70%	3	3.90%	4	1.40%	2	2.60%	2	3.20%	4	1.30%
	One	44	12.20%	5	6.60%	29	10.20%	15	19.20%	8	12.70%	36	12.00%
	Two	236	65.20%	33	43.40%	194	68.30%	42	53.80%	47	74.60%	189	63.20%
	Three	76	21.00%	35	46.10%	57	20.10%	19	24.40%	6	9.50%	70	23.40%
	p					0.053				0.045*			

*significant at $p<0.05$.

Table 3 Screening for osteoporosis and treatment in the high risk groups

		Gender			
		Male >70years		Female>65years	
		n	%	n	%
Screening tests					
Vitamin D level	Done	3	100.00%	41	95.30%
Calcium Level	Done	0	0.00%	0	0.00%
ALP level	Done	3	100.00%	43	100.00%
Phosphate level	Done	3	100.00%	40	93.00%
Magnesium level	Done	0	0.00%	25	58.10%
Albumin Level	Done	3	100.00%	43	100.00%
Creatinine level	Done	3	100.00%	40	93.00%
PTH level	Done	0	0.00%	19	44.20%
TSH level	Done	0	0.00%	39	90.70%
DEXA Scan	Done	2	66.70%	32	74.40%
Prophylaxis/treatment					
Calcium	Yes	2	66.70%	38	88.40%
Vitamin D	Yes	3	100.00%	30	69.80%
Bisphosphonate	Yes	1	33.30%	17	39.50%
Number of drugs	None	0	0.00%	3	7.00%
	One	0	0.00%	8	18.60%
	Two	3	100.00%	19	44.20%
	Three	0	0.00%	13	30.20%

Table 4 Binomial logistic regression model to define characteristics of patients at risk of not having DEXA scan

	p	Adjusted odds ratio	95% C.I. for odds ratio	
			Lower	Upper
Age	<0.001*	0.957	0.942	0.972
Gender (Female)	0.08	0.564	0.298	1.071
BMI	<0.001*			
Normal	<0.001*	18.11	5.003	65.555
Overweight	<0.001*	22.615	5.991	85.365
Obese	<0.001*	20.295	5.442	75.681
Extremely obese	<0.001*	17.744	4.51	69.818
Dose (7mg)	0.052	0.542	0.292	1.005
Duration	0.109			
3-6months	0.078	4.247	0.851	21.201
>6-12months	0.223	2.018	0.653	6.24
>12-24months	0.853	1.102	0.394	3.08
>24months	0.293	2.29	0.488	10.74

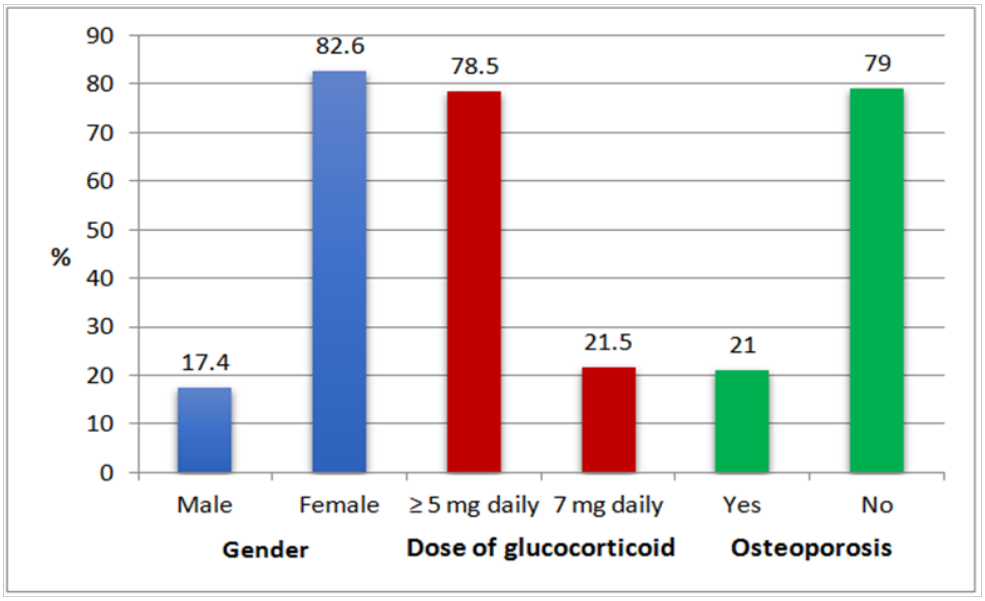

Figure 1 Gender, dose of prednisolone, and prevalence of osteoporosis in the studied patients.

Citation: Al-Aidarous S, Al-Husayni F, Alzahrani J, et al. Osteoporosis screening for patients with prolonged use of glucocorticoid in national guard hospital – Jeddah, Saudi Arabia. *Endocrinol Metab Int J.* 2019;7(4):113–120. DOI: 10.15406/emij.2019.07.00254

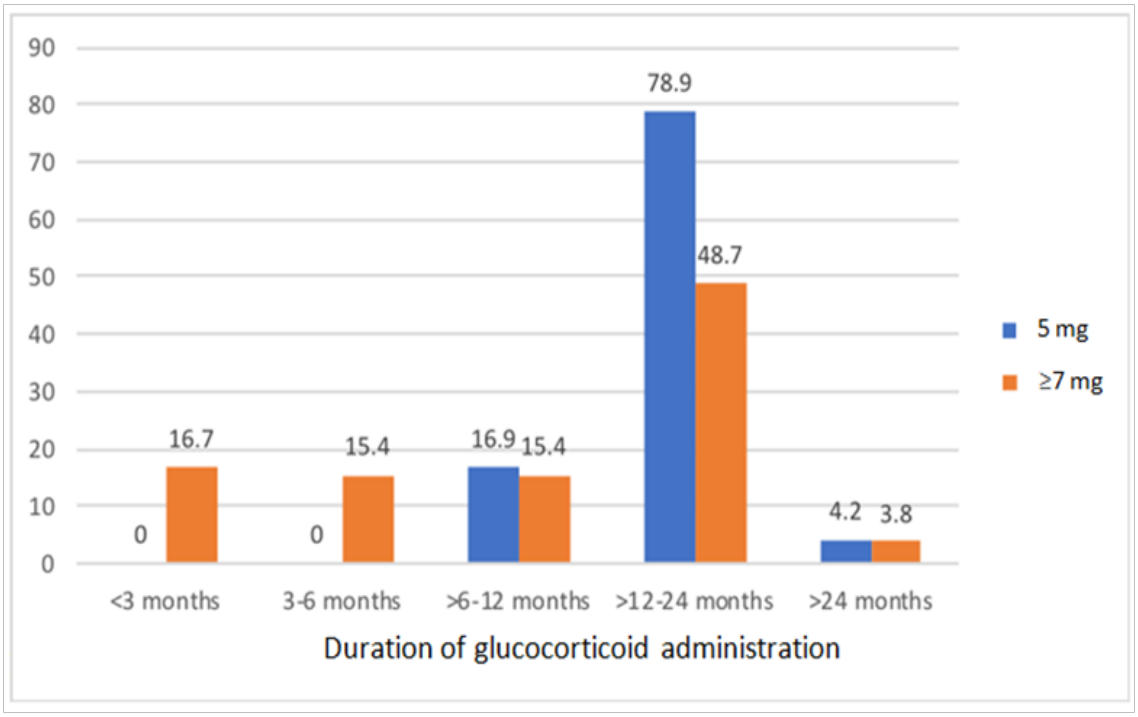

Figure 2 Dose and duration of prednisolone treatment in the studied patients.

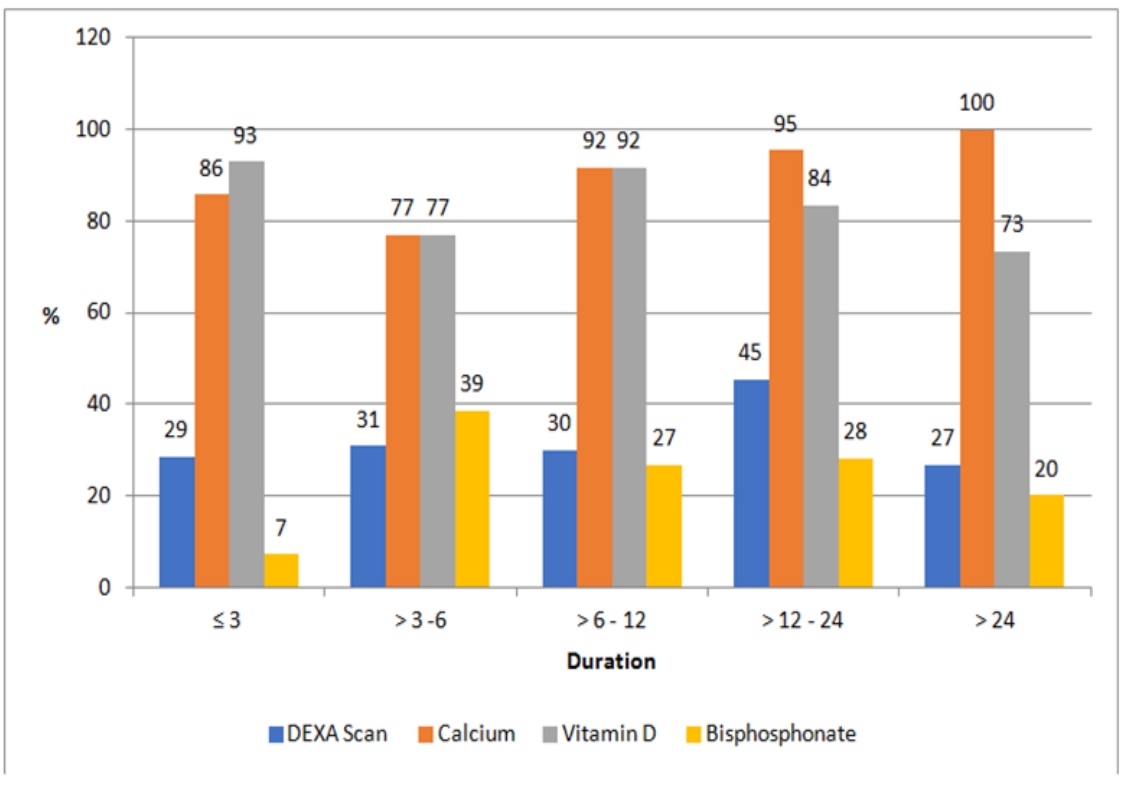

Figure 3 The duration of prednisolone use, DEXA scan, and medications.

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Discussion

In Saudi Arabia, osteoporosis affects about one third of women and men aged 50-79years.[4] Chronic glucocorticoid administration ranks as the first secondary cause of osteoporosis at any age.[1,14] Screening for osteoporosis is of paramount importance in patients taking glucocorticoids for long durations; and many guidelines have been developed to define methods and plans for screening.[15] There is a paucity of studies in Saudi Arabia that address this important topic; only one study was carried out in King Fahd Hospital, Al-Khobar.[16] Therefore, the present study aimed to assess if patients with prolonged use of steroids are checked for osteoporosis in National Guard Hospital, Jeddah.

Bone densitometry is recommended in patients on long term use of steroids and T-score of −1.5 or lower indicates the need for intervention with a bone-sparing agent, for example bisphosphonates.[17,18] The most frequently performed tests in this study included levels of albumin (99.2%), alkaline phosphatase (98.6%), vitamin D (95%), and creatinine (93.6%). The least performed test was calcium level (1.1%). DEXA Scan was done in 40.9% of patients; independent of the dose or duration of steroids or the patients' gender. These percentages are higher than those reported in previous studies.[16,19] A similar rate of DEXA scanning (43.4%) was reported by Erb et al.[20] In high risk cases, rates of DEXA scan were still suboptimal as the Saudi Osteoporosis Society recommended that all Saudi women above the age of 60years must undergo a BMD assessment using DEXA.[21]

Good nutrition, an adequate dietary intake of calcium and vitamin D, appropriate physical activity, avoidance of tobacco and alcohol should be considered for subjects receiving steroids for 3months or more.[17,18] The Effective, first-line management therapies for the prevention and treatment of glucocorticoid-induced osteoporosis include calcium and vitamin D.[22,23] The American College of Rheumatology (ACR) stated in its guideline that supplementation with calcium and vitamin D, or an activated form of vitamin D, should be offered to all patients receiving glucocorticoids, to restore normal calcium balance. This combination has been shown to maintain bone mass in patients receiving long-term low-to-medium-dose glucocorticoid therapy who have normal levels of gonadal hormones.[24] The majority of patients in this study followed this standard as calcium and vitamin D were administered in 93.9% and 84.5% of cases, respectively. Moreover, ACR recommended also treatment with bisphosphonate to prevent bone loss in all men and postmenopausal women in whom long-term glucocorticoid treatment at ≥5mg/day is being initiated. Bisphosphonate was administered in only 27.1% of total cases in our study. A study by Sadat-Ali et al.[16] in al-Khobar stated that none of their patients received bisphosphonate at all. However, similar studies were conducted and reported higher rates of bisphosphonates (35.3%-40%) use than ours.[25,26] The number of patients who did not receive any treatment in this study was 6 (1.7% of total cases) which was less than the percentage of 14% reported by Erb et al.[20] However, three of them were diagnosed with osteoporosis, which raises concern about the neglect of prophylaxis then treatment in these cases.

Overall, the adherence to well-recognized recommendations for prophylaxis/treatment of GIOP in the present study was satisfactory to a large extent, as the percentage of patients who received at least one medication exceeded 80% (which is the percentage adopted by most audits). Much lower rates were reported by other older studies and audits. In the UK, Peat and colleagues reported that only 6% of their patients were receiving any osteoporosis medication.[27] In another survey from the UK, 14% of patients had received treatment for the prevention of osteoporosis.[28] In a study in the US, 29% of patients received some medication for osteoporosis.[29] These much higher adherence rates in our study could be explained by the nature and location of this study which was conducted in one center, while many of the other studies were multi-center. Another factor also - that was unfortunately not investigated in this study - was the specialties of the treating doctors; as it was suggested that some subspecialties show more adherence than the others.[30] There was no trend in rates of treatment with prescription medications for osteoporosis across glucocorticoid dosage-duration categories; an observation shared by Solomon et al.[30] However, in the current study there seemed to be a neglect of the importance of bisphosphonates, particularly in at risk patients. Also, 7% of women above 65years had no drugs at all.

We then attempted to define the characteristics of patients at risk of not having DEXA scan, while being on long term steroid therapy. Increase in age was associated with a decreased risk (patients were more likely to have DEXA scan); while patients with increased BMI were more likely to not have DEXA scan, compared to the underweight. However, Solomon et al.[30] reported that men and premenopausal women were significantly more likely to not undergo bone densitometry and not receive prescription osteoporosis treatment.

Conclusion

The rates of DEXA Scan performance were suboptimal. Treatment received by the patients on chronic steroid medications is satisfactory to a large extent. However, doctors' awareness should be raised as regards patients at high risk of developing GIOP and the appropriate use of bisphosphonates. Many guidelines are available to help doctors monitor patients at risk of GIOP and prescribe prophylaxis/treatment medications. We recommend developing National Saudi Guidelines for management of GIOP that should be distributed to all health care facilities that manage those patients. Further audits should be carried out at health care facilities to record and ensure adherence to the guidelines.

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Conflicts of interest

The authors declare that there are no conflicts of interest.

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