ORIGINAL ARTICLE

CONTENTS

Vitamin D status as a laboratory marker of whole spectrum of severity of osteoarthritis of knee

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ABSTRACT

Aim: The aim of our research is to examine any relationship between vitamin D status and knee osteoarthritis.

Materials and Methods: A specimen of 160 individuals presented to medical services in outpatient doctor's office were recruited into evaluations 80 participants with established diagnosis of osteoarthritis of knee chosen as cases and 80 participants without clinical and radiological evidence of knee joint osteoarthritis chosen as controls, both were assessed by meticulous clinical and rheumatologic examination, radiological assessment, and vitamin D quantification. Diagnosis of cases was verified in accordance with American college of rheumatology criteria, for whom both pain and radiological severity were measured.

Results: mean age is 69.2570, 96 females, 64 males. F: M ratio is 1.5:1, 85 had subnormal vitamin D while 75 had normal vitamin D level. Majority who were vitamin D insufficient belong to cases 83.5%. Majority of those who have adequate vitamin D level related to control group with significant association P-value 0.0001. Most of cases who were vitamin D insufficient 60 out of 71 have grade 3 and 4 kellegren-Lawrence score of radiological severity with significant association where p-value 0.001, 14 out of 71 and 50 out of 71 case who have vitamin D inadequacy suffering from moderate and severe pain by visual analogue scale subsequently with significant association P value 0.001.

Conclusions: vitamin D status had substantial relation with various aspects of severity and perhaps worsening of knee osteoarthritis, emphasizing necessity of promoting the vitamin D quantification in those patients.

KEY WORDS: vitamin D, laboratory marker, spectrum of severity

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INTRODUCTION

The prevalence of both vitamin D and knee osteoarthritis is rapidly increasing among older adults, and the two conditions often coexist, but whether traditional relationships exist between them is a matter of debate. Osteoarthritis of knee is the degenerative disorder that targeted chiefly geriatric public, knee is the most often affected joint by this substantively disabling illness [1]. It affects all architectural components of joints predominantly cartilaginous parts [2]. Beside to the degenerative part of osteoarthritis, there is an exist evidence of appreciable inflammatory background in this popular handicapping disorder [3]. Osteoarthritis of the knee is an extremely common disease that has an increasing prevalence worldwide, is slightly higher in women and has a negative impact on lifestyle, leading to significant financial hardship. [4]. Vitamin D inadequacy is dominant globally, remarkably in Asian countries, rendering this metabolic disturbance had notable health burden in those nations [5]. Both osteoarthritis and vitamin D insufficiencies are common health troubles in elder public [6]. It is obvious that vitamin D is crucial for maintenance of elemental bone minerals that make up bone. Vitamin D can diminish the turnover of both bone and cartilage degradation and decelerate the progression of knee osteoarthritic pathogenesis, for that justification scarce vitamin D reserve negatively impacting the wellbeing of both cartilage and bone metabolic environment and therefore most pathogenetic facets of osteoarthritis [7]. Vitamin D also attenuates the inflammatory elements of knee osteoarthritis [8]. Low vitamin D levels correlate with a reduction in all clinical and pathogenetic aspects of osteoarthritis, including structural deterioration and functional disability [9]. Research findings on the association between vitamin D deficiency and knee osteoarthritis are controversial regarding its connections to pathogenesis, but plenty of reviews exhibit its causation and link with various aspects of this disease [10].

AIM

The aim of our research is to examine any relationship between vitamin D status and knee osteoarthritis across the spectrum of severity and clinical features. We hypothesize that vitamin D status is relevant to knee osteoarthritis and influences various aspects of this common disabling disease, so that easily applicable appropriate testing and therefore supplementation may help alleviate and slow the progression of this crippling disease.

MATERIALS AND METHODS

TYPE OF STUDY

A case-control study, which was extended from the beginning of the first week of December 2020 to the end of the last week of May 2021.

STUDY POPULATION

The candidates account a list of patients seeking outpatient care at a physician's office in Al-Hussein teaching hospital in Al-Nasiriya city. The total number of participants recruited for analysis were 160, with 80 cases was chosen as osteoarthritis of knee, and 80 candidates who were lacking pain elected as control, they were assured have no clinical and radiological evidence of osteoarthritis of knee.

EXCLUSION CRITERIA

- Anyone with neurological weakness of lower limbs.
- Anyone with incapacitating incurable illness comprising hematological and solid cancers.
- Anyone notable to have metabolic bone disease.
- Anyone consuming vitamin D supplements.
- Anyone consuming painkiller in the antecedent week.
- Anyone diagnosed with degenerative (of additional joints other than knee) and autoimmune illnesses involving rheumatoid arthritis.

The sample size was reasonable, limited by the availability of patients and the time frame of the study. Regarding the selection of control samples, a systematic random sampling action plan was carried out to select control samples.

ETHICAL CONCERN

An ethical affirmation was obtained from Al-Hussein teaching administrative authorities, an informed consent was obtained from all participators.

STUDY TOOLS

The questionnaire. To collect the data, a special questionnaire model was developed, which was tested and evaluated by three experienced persons (a community medicine specialist and a physician) to check the validity of the questionnaire. The questionnaire consist of two subdivisions:

First subdivision: all-data pertinent to identity (age, gender, job, residency, education, and marital state).

Second subdivision: all-data involving the inquiry related to manifestations of knee joint linked to osteoarthritis applicable to criteria of American college of rheumatology, duration of manifestations, preexistent comorbidities, drugs, and severity of pain.

DIAGNOSTIC PROCEDURES

In both the case and control groups, the condition of the musculoskeletal system of the knee joint was assessed. Weight and height were measured for all participators and body mass index (BMI) were calculated for all candidates in study category. In both the cases and control were sub classified into a group with a body mass index above normal when it was above 25, and a group with an index within normal limits when it was below 25 [23]. X-ray of knee joint was undertaken for both cases and control in two viewpoint both anteroposterior and lateral and interpreted by radiologist make blind to clinical background of patients and kellegren score was measured from x -rays that exhibits characters of osteoarthritis [24]. Severity of pain for cases were verified by visual analogue scale and the intensity of pain was classified as mild (5-44 mm), moderate (45-74 mm) and, severe (75-100 mm) [11]. All cases match criteria of American college of rheumatologist and the number of criteria was ascertained [12]. Those participators who lacks pain (0-4 mm on visual analog scale), had normal findings on clinical checking and devoid radiological signs of osteoarthritis were elected as control. Vitamin D was quantified for all candidates and the study grouping were classified into normal when measure above 50 nanomole per liter, and subnormal when the measure underneath 50 nanomole per liter [13].

STATISTICAL ANALYSIS

Statistical package of social sciences (SPSS) version 25 was utilized for data assay, descriptive statistics, frequencies, percentages, associations, tests of significance (Chi-square, Fischer-exact test, T-test, and ANOVA test) was utilized for clarification for categorical variables, means and standard deviation were utilized to submit statistics of continuous variables. A p-value underneath 0.05 was stated as statistically significant.

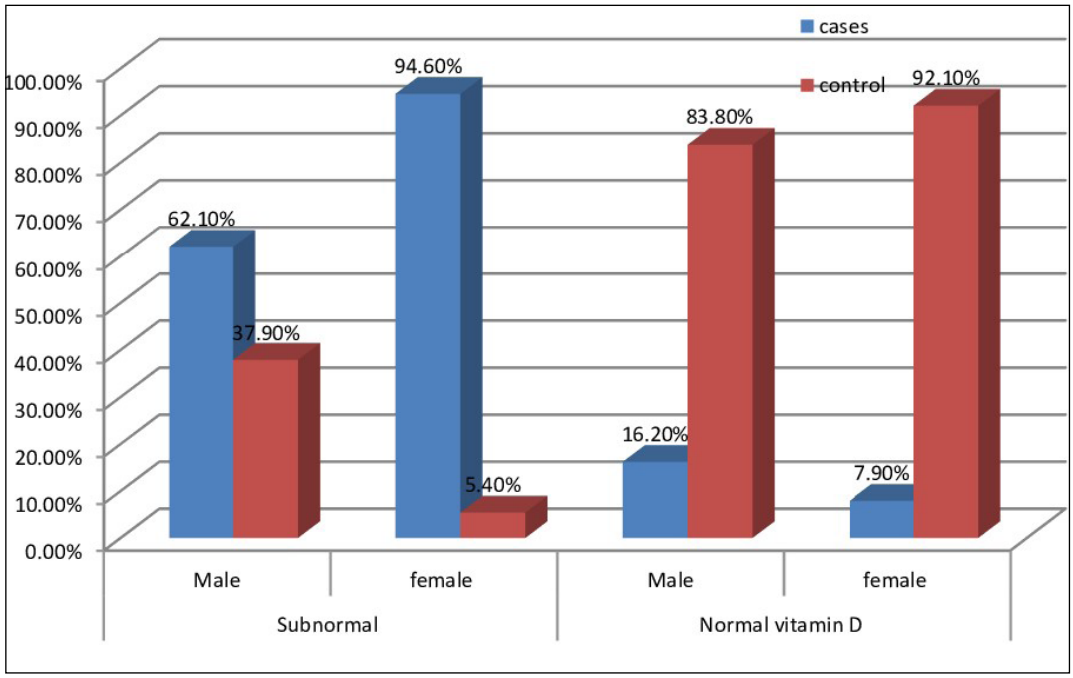

Fig. 1. Cases versus controls matched for gender and vitamin D status: Chi square for cases = 14.735, P value=0.005, OR=0.089; Chi square for control =1.228, P value=0.268, OR=1.258.

Table 1. Distribution of vitamin D among studied population

		Cases	Control	Total	Chi-square	P value	Odds ratio
Vitamin D	Subnormal	71	14	85	81.544	0.0001	37.190
		83.5%	16.5%	100.%			
	Normal	9	66	75			
		12.0%	88.0%	100.%			
Total	No.	80	80	160			
		50.0%	50.0%	100.%			

Table 2. Distribution of knee osteoarthritis severity in relation to vitamin D status

		Vitamin D		Total	Chi-square	P value
		Subnormal	Normal			
Kelly-green score	0.00	14	66	80	92.880	0.0001
		17.5%	82.5%	100.0%		
	1.00	6	7	13		
		46.2%	53.8%	100.0%		
	2.00	5	0	5		
		100.0%	0.0%	100.0%		
	3.00	25	1	26		
		96.2%	3.8%	100.0%		
	4.00	35	1	36		
		97.2%	2.8%	100.0%		
Total	Count	85	75	160		
	%	53.1%	46.9%	100.0%		

RESULTS

A total of 160 contributors included within the analysis, distributed equally into two group: osteoarthritis of knee appointed as cases and those contributors who devoid radiological and clinical signs of knee osteoarthritis appointed as control. The mean age of total sample was 69.2570, 96 female 64 male (with F: M ratio 1.5:1) those contributors who were insufficient in vitamin D (85) were older mean age = 70.8353 than those who were sufficient in vitamin

Table 3. Distribution of knee osteoarthritis severity according to vitamin D status amongst cases only

		Vitamin D		Total	Chi-square	P value
		Subnormal	Normal			
Kelly-green score	1.00	6	7	13	28.274	0.001
		46.2%	53.8%	100.0%		
	2.00	5	0	5		
		100.0%	0.0%	100.0%		
	3.00	25	1	26		
		96.2%	3.8%	100.0%		
	4.00	35	1	36		
		97.2%	2.8%	100.0%		
Total	Count	71	9		80	
	%	88.8%	11.3%		100.0%	

Table 4. Distribution of pain intensity on a visual analogue scale according to the level of vitamin D in patients

		Vitamin D		Total	Chi-square	P value
		Subnormal	Normal			
Severity	Mild	7	8	15	38.260	0.001
		46.7%	53.3%	100.0%		
	Moderate	14	1	15		
		93.3%	6.7%	100.0%		
	Severe	50	0	50		
		100.0%	0.0%	100.0%		
Total 88.8%		71	9	80		
		11.3%	100.0%			

D (75) mean age = 67.5067. Regarding the gender distribution among cases and controls as indicated by vitamin D levels, there is a significant association at P value=0.005 (Fig.1).

Most of the cases (83.5%) had subnormal vitamin D level (71 cases) while only 9 (12%) patients had vitamin D level within normal range while most of the control group (88%) had normal vitamin D level (66 cases) while only 14 (16.5%) had subnormal vitamin D level; out of the total sample 85 participants had subnormal vitamin D level (53.1%) while 75 participants had normal vitamin level (46.9%) with significant association between vitamin D status and knee osteoarthritis where P value = 0.0001 (Table 1).

Of the 80 control subjects, 66 had normal vitamin D while 14 have subnormal vitamin D level. Of the 80 knee osteoarthritis cases, 13 belong to severity score one, 6 have subnormal vitamin D while 7 have normal level, five participants belong to category two all of them have subnormal level, 26 belong to category 3 of whom just one have normal level meanwhile 36 belong to score four of whom just one have normal level while 35 participants have subnormal level. There is significant association between vitamin D measure and radiological grade of severity of OA of knee, where P value=0.0001 (Table 2).

There is significant relationship between the radiological severity of knee osteoarthritis and vitamin D measure as the following clarification: out of 80 cases who suffer from osteoarthritis of knee, there is 13 cases belong to score one, of whom 7 had normal level while 6 had subnormal level. All 5 participants who belong to grade two of severity had subnormal vitamin D level, 25 out of 26 participants who belong to grade three have subnormal level while 35 out of 36 who belong to grade four have subnormal level with significant association between vitamin D measure and severity of osteoarthritis of knee (p value=0.001) as displayed in Table 3.

Majority of cases who have had inadequate vitamin D suffer moderate and severe pain, in contrast to cases who have adequate vitamin D where they suffer mild pain with significant association between severity of pain as stated by pain analogue scale and osteoarthritis where P value-0.001as the following clarifications: 15 participants belong to mild category of pain severity of whom 8 had normal vitamin measure while 7 had subnormal level,15 belong to moderate severity category,

Table 5. Cases with insufficient vitamin D levels

		N	Mean	Std. Deviation	ANOVA	Sig.
Age (all)	Subnormal	85	70.8353	7.58891	6.505	0.012
	Normal	75	67.5067	8.91760		
	Total	160	69.2750	8.37933		
Duration of OA in months	Subnormal	71	19.3803	7.69483	16.447	0.000
	Normal	9	8.8889	1.76383		
	Total	80	18.2000	7.99430		
Age (cases)	Subnormal	71	70.6056	7.44212	5.986	0.017
	Normal	9	63.5556	12.72901		
	Total	80	69.8125	8.39695		

of whom just one had normal level. all 50 participants who belong to severe category have inadequate level with significant association between vitamin D level and pain severity (Table 4).

Cases with osteoarthritis of knee with insufficient vitamin D had long-lasting duration of symptoms relative to cases with sufficient vitamin D status with significant association where p value=0.000. The 85 participants in the total sample who had subnormal levels were older (mean age 70.8353) with a significant association where p value = 0.012 between age and vitamin D level. Most of those cases 71 out of 80 had subnormal levels were older with a mean age = 70.6056 while only 9 with normal levels had a mean age of 63.5556 with a significant association where p value = 0.017 (Table 5).

There is remarkable association in relation to number of morbidities and vitamin D state amongst cases where P value=0. 011. There is remarkable association amongst hypertension, diabetes, cardiac diseases, hyperlipidemia, obesity and vitamin D state where P values=0.008, 0.002, 0.011, 0.034, 0.016 sequentially, as displayed in Table 6.

DISCUSSION

In our study, we approach to crucial findings: the majority of cases (83.5%) asserted to be osteoarthritis of knee was found to have vitamin D depletion, in contrast to control participants who lacks osteoarthritis of knee 16.5% had subnormal vitamin D, and diverse studies explore increasing prevalence of vitamin D inadequacy among patients who have had osteoarthritis of knee [14]. Most of cases in our sample who were deficient in vitamin D have had high-ranking radiological severity as stated by kellegren score 60 out of 71 with significant association where P value 0.001. Our detection is concordant with Hasan Anari et al. [15], who found that patients with knee osteoarthritis who have scarce vitamin D having higher radiological grade of severity. Further crucial determination is that substantial number of patients who were vitamin D insufficient have more severe pain as the principal manifestation of knee osteoarthritis. A cohort study designated as cross-sectional study conducted in United Kingdom found a significant association amongst knee osteoarthritis and knee pain [16]. This findings might have a therapeutic significance concerning the implementation of vitamin D supplementation on amelioration of cardinal symptoms of knee osteoarthritis principally pain and functional disability as studied by diverse analyses [17]. Cases with confirmed osteoarthritis of knee who are vitamin D insufficient were older(mean age 70.6056) and this is closely in compatibility what was detected by JA Jansen and FS Haddad [18] who displayed that vitamin D deficiency have had high prevalence in geriatric population with knee osteoarthritis. Those candidates who have had deprivation in vitamin D state in our assay were older than those who had adequate vitamin reserve emphasizing the exceedingly valuable information that vitamin D deficiency is more dominating in geriatric public with statistical significance (P value=0.017) and our determination in accordance with Niamh Aspell et al. [19]. Chinghai Ding et al [20] realize that shortage of vitamin D might be a anticipator of degenerative architectural alterations in knee joint in senile adults. Noteworthy higher number of widespread morbidities having dominance in cases influenced with vitamin D deficiency, particularly hypertension, diabetes, cardiac disease, hyperlipidemia, and obesity were strongly interconnected with vitamin D deficiency (P values 0.008, 0.002, 0.011, 0.034, 0.016) respectively. A variety of analyzed reviews illuminate powerful interrelation of vitamin D deficiency with a heterogeneous co-morbid disorders [21,22]. Our analysis had particular limitations, initially greater size is required to explore more potent association of vitamin D status causally with a heterogeneous facets of clinic pathological

Table 6. Differences in vitamin D conditions among cases and control in accordance with some determinants

Determinants		Cases			X^2, P, odds R	Control			X^2, P, odds R
		Subnor.	Nor.	Total		Subnor.	Nor.	Total	
Morbidity	.00	1	1	2	18.738, 0.011	0	14	14	69.226 0.001
		50.0%	50.0%	100.0%		0.0%	100.0%	100.0%	
	1.00	2	2	4		0	28	28	
		50.0%	50.0%	100.0%		0.0%	100.0%	100.0%	
	2.00	6	3	9		0	17	17	
		66.7%	33.3%	100.0%		0.0%	100.0%	100.0%	
	3.00	10	2	12		2	7	9	
		83.3%	16.7%	100.0%		22.2%	77.8%	100.0%	
	4.00	19	1	20		10	0	10	
		95.0%	5.0%	100.0%		100.0%	0.0%	100.0%	
	5.00	33	0	33		2	0	2	
		100.0%	0.0%	100.0%		100.0%	0.0%	100.0%	
hypertension	No	15	6	21	8.557 0.008 0.143	4	45	49	7.563 0.007 0.187
		71.4%	28.6%	100.0%		8.2%	91.8%	100.0%	
	Yes	56	3	59		10	21	31	
		94.9%	5.1%	100.0%		32.3%	67.7%	100.0%	
Diabetes mellitus	0	14	6	20	9.390 0.002 0.123	0	51	51	29.843 0,001 1.933
		70.0%	30.0%	100.0%		0.0%	100.0%	100.0%	
	1	57	3	60		14	15	29	
		95.0%	5.0%	100.0%		48.3%	51.7%	100.0%	
Heart disease	0	18	6	24	6.324 0.011 0.170	2	52	54	21.905 0.001 0.045
		75.0%	25.0%	100.0%		3.7%	96.3%	100.0%	
	1	53	3	56		12	14	26	
		94.6%	5.4%	100.0%		46.2%	53.8%	100.0%	
Hyperlipidemia	No	16	5	21	4.499 0.034 0.233	1	59	60	41.753 0.001 2.813
		76.2%	23.8%	100.0%		1.7%	98.3%	100.0%	
	Yes	55	4	59		13	7	20	
		93.2%	6.8%	100.0%		65.0%	35.0%	100.0%	
Obesity	1.00	7	4	11	8.056 0.016 0.137	8	40	48	0.058 0.277 0.867
		63.6%	36.4%	100.0%		16.7%	83.3%	100.0%	
	2	64	5	69		6	26	32	
		92.8%	7.2%	100.0%		18.8%	81.3%	100.0%	
Total		71	9	80		14	66	80	
percentage		88.8%	11.3%	100.0%		17.5%	82.5%	100.0%	

range of osteoarthritis of knee, hormonal checking including parathyroid hormone was not achieved because of restricted capacity and accessibility in our hospital to shed light on the influence of vitamin D insufficiency on bone and cartilage turnover with resultant causal impacts. Further research and studies of bigger size are necessary in the future incorporating the probable beneficial impact of vitamin D on alleviating all aspects of knee osteoarthritis [23, 24].

CONCLUSIONS

Vitamin D status had substantial relation with various aspects of severity and perhaps progression in osteoarthritis of knee. The insufficiency of vitamin D in cases of osteoarthritis of knee is prevalent specifically in comorbid elder patients with long duration of illnesses, inadequate level of vitamin D. It is substantially linked to increasing severity both radiologically and clinically as evidenced by increased pain severity.

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CONFLICT OF INTEREST

The Authors declare no conflict of interest

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