Association between CRP with progression of knee osteoarthritis:

case-control study

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Didecation

We dedicate our research to our families who have supported us all these years.

We extend our full thanks and appreciation to the supervisor of our research, the head of the Department of Internal Medicine, ***Dr. Haider Shaheed****, for his scientific efforts and opinions and observation that enriched the research to appear in the current image ,which without his supervision, we would not have been able to complete it. We also thank* ***Dr. Ali Abd Saadoun*** *for helping us complete our research, thanks to his commendable efforts.*

Abstract

Backround and objective: Osteoarthritis is the most common cause of joint disease and one of the leading cause of disability it is the most prevalent disease in our society with worldwide distribution.

Aim of study: Association between CRP with progression of knee osteoarthritis :case-control study in Thi-qar.

Method and material: Data from 75 participants were enrolled from 20 0f November ,2021 to 21 of February ,2022 in Al-Nasiriyah Teaching Hospital in Dhi-Qar ,Iraq. Data were divided into two groups. The cases included 43 were compared with 32 healthy individuals as a control group and matched for age, sex, and BMI of patient's group and CRP and radiological assessment.

Results: CRP was positive in 14 out of 43 of knee osteoarthritis patients compared to 1 out of 32 of healthy controls . CRP positive among knee OA and significant associated with age,site of joint, duration of knee OA, severity, presence of crepitus and x ray finding (p value<0.05) .

No significant association with gender, family history, drug history, and BMI (p value>0.05).

Conclusion: CRP positive was significant association with knee osteoarthritis patients compared with healthy control .

Introduction

(OA) is the most common degenerative joint disease, affecting more than 25% of the population over 18 years-old. And is the most common form of arthritis and one of the leading causes of disability. And It is the most prevalent disease in our society, with a worldwide distribution.

It was believed that OA was exclusively a degenerative disease of the cartilage, however, latest evidence has proven that OA is a multifactorial entity, involving multiple causative factors like trauma, mechanical forces, inflammation, biochemical reactions, and metabolic derangements.

CRP is produced by the liver. The level of CRP rises when there is inflammation throughout the body. It is one of a group of proteins called acute phase reactants that go up in response to inflammation.

Prevalence

About 13% of women and 10% of men aged 60 years and older have symptomatic knee OA. The proportions of people affected with symptomatic knee OA is likely to increase due to the aging of the population and the rate of obesity or overweight in the general population. . During a one year period, 25% of people over 55 years may demonstrate persistent episode of knee pain, in whom about one in six have to consult their general practitioner about it in the same time period. About 10% of people aged over 55 years have painful disabling knee OA of whom one quarter are severely disabled. . Prevalence of knee OA in men is lower compared with women .This was shown in a meta analysis of males and females in which the incidence of knee OA in males aged <55 years was lower than females.

Females, particularly those ≥55 years, tended to have more severe OA in the knee but not in other sites.

Mehods

This case-control study was conducted in the Department of Rheumatology in Al-Nasiriyah Teaching Hospital in Dhi-Qar ,Iraq.

Data from 75 participants were enrolled from 20 0f November ,2021 to 21 of February ,2022.

Data were divided into two groups. The cases included 43 were compared with 32 healthy individuals as a control group and matched for age, sex, and BMI of patient's group.

Patients with any of the following were excluded: other etiologies like infectious diseases, cancer, inflammatory rheumatic diseases such as rheumatoid arthritis, connective tissue diseases, gout, and others, acute coronary heart disease, metabolic disorders (like diabetes), liver failure, renal failure, pregnancy.

Full history was taken from all individuals including: age, sex, site of knee OA (unilateral or bilateral), duration of disease(<1year or >1year) , knee pain severity (none,mild,moderate,sever), presence of crepitus, family history of knee OA, history of drug intake, and clinical examination was done all participants.

BMI was calculated by the equation BMI =weight (kg) /height (m2) ,and then classified according to BMI into BMI <25 kg/m2, BMI≥25kg/ m2.

And bilateral knee x ray was done as AP and lateral views(for findings narrowing joint space ,osteophyte formation and subchondral sclerosis).

CRP investigation (if result of analysis positive or negative) for both cases and control.

Statistical analysis was done by entering the data on the computer using Microsoft Excel.

The results analysis by using ANOVA, p value ,Chi square test.

Results

Age according to CRP

age				ANOVA, P
CRP	Mean	N	Std. Deviation	
.00	45.0000	60	13.71131	7.632
1.00	55.5333	15	10.83557	0.007
Total	47.1067	75	13.78755	

gender * CRP

Crosstab

			CRP			
			.00	1.00	Total	Pearson Chi-Square, p value
gender	1.00	Count	22	5	27	.058[a]
		% within CRP	36.7%	33.3%	36.0%	.810
	2.00	Count	38	10	48	
		% within CRP	63.3%	66.7%	64.0%	
Total		Count	60	15	75	
		% within CRP	100.0%	100.0%	100.0%	

site * CRP

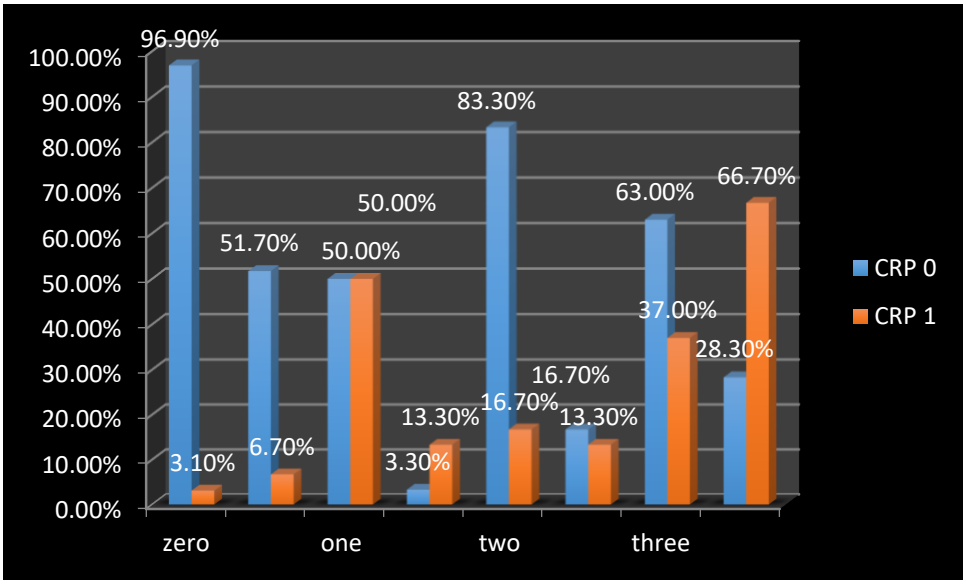
Crosstab

			CRP			Pearson Chi-Square, p value
			.00	1.00	Total	
site	.00	Count	31	1	32	9.942[a]
		% within CRP	51.7%	6.7%	42.7%	0.008
	1.00	Count	10	5	15	
		% within CRP	16.7%	33.3%	20.0%	
	2.00	Count	19	9	28	
		% within CRP	31.7%	60.0%	37.3%	
Total		Count	60	15	75	
		% within CRP	100.0%	100.0%	100.0%	

duration * CRP

Crosstab

			CRP			Pearson Chi-Square, p value
			.00	1.00	Total	
duration	.00	Count	31	1	32	10.323[a]
		% within CRP	51.7%	6.7%	42.7%	.006
	1.00	Count	10	6	16	
		% within CRP	16.7%	40.0%	21.3%	
	2.00	Count	19	8	27	
		% within CRP	31.7%	53.3%	36.0%	
Total		Count	60	15	75	
		% within CRP	100.0%	100.0%	100.0%	



severity * CRP

Crosstab

			CRP			Pearson Chi-Square, p value
			.00	1.00	Total	
severity	.00	Count	31	1	32	12.927[a]
		% within CRP	51.7%	6.7%	42.7%	0.005
	1.00	Count	2	2	4	
		% within CRP	3.3%	13.3%	5.3%	
	2.00	Count	10	2	12	
		% within CRP	16.7%	13.3%	16.0%	
	3.00	Count	17	10	27	
		% within CRP	28.3%	66.7%	36.0%	
Total		Count	60	15	75	
		% within CRP	100.0%	100.0%	100.0%	

cripitus * CRP

Crosstab

			CRP			Pearson Chi-Square, p value
			.00	1.00	Total	
cripitus	.00	Count	38	5	43	4.415[a]
		% within CRP	63.3%	33.3%	57.3%	.036
	1.00	Count	22	10	32	
		% within CRP	36.7%	66.7%	42.7%	
Total		Count	60	15	75	
		% within CRP	100.0%	100.0%	100.0%	

familyHx * CRP

Crosstab

			CRP			Pearson Chi-Square, p value
			.00	1.00	Total	
familyHx	.00	Count	44	13	57	1.170[a]
		% within CRP	73.3%	86.7%	76.0%	.279
	1.00	Count	16	2	18	
		% within CRP	26.7%	13.3%	24.0%	
Total		Count	60	15	75	
		% within CRP	100.0%	100.0%	100.0%	

drugHx * CRP

Crosstab

			CRP			Pearson Chi-Square, p value
			.00	1.00	Total	
drugHx	.00	Count	39	9	48	.130[a]
		% within CRP	65.0%	60.0%	64.0%	.718
	1.00	Count	21	6	27	
		% within CRP	35.0%	40.0%	36.0%	
Total		Count	60	15	75	
		% within CRP	100.0%	100.0%	100.0%	

BMI * CRP

Crosstab

			CRP			Pearson Chi-Square, p value
			.00	1.00	Total	
BMI	1.00	Count	24	3	27	2.083[a]
		% within CRP	40.0%	20.0%	36.0%	0.230
	2.00	Count	36	12	48	
		% within CRP	60.0%	80.0%	64.0%	
Total		Count	60	15	75	
		% within CRP	100.0%	100.0%	100.0%	

Xray * CRP

			CRP			
			.00	1.00	Total	
Xray	.00	Count	31	1	32	18.350
		% within CRP	51.7%	6.7%	42.7%	0.001
	1.00	Count	21	6	27	
		% within CRP	35.0%	40.0%	36.0%	
	2.00	Count	8	6	14	
		% within CRP	13.3%	40.0%	18.7%	
	3.00	Count	0	2	2	
		% within CRP	0.0%	13.3%	2.7%	
Total		Count	60	15	75	
		% within CRP	100.0%	100.0%	100.0%	

DISSCUSION:

Table 1: Age associated to CRP has shown The mean and SD for -ve CRP(N=60) were (45.0,13.71) respectively and P(7.632) so there is no association between them.

While mean and SD for +ve CRP(N=15) were (55.53,10.83) respectively and P(0.007) so there is significant association between them.

Table 2: gender associated to CRP has shown most of the participants in both groups(case, control) were female (64%).

For male in both groups (N=27) the results were 22 of them have –ve CRP and 5 have +ve CRP. While female in both groups (N=48) the result were 38 of them have –ve CRP and 10 have +ve CRP.

Pvalue(0.810) so there is no association between CRP and gender.

Tabel3: site of knee OA associated to CRP

Result has shown Unilateral knee OA (N=15), 10 of them have –ve CRP and 5 of them have +ve CRP.

While bilateral knee OA (N=28) , 19 of them have –ve CRP and 9 of them have +ve CRP.

P value(0.008) So there is significant association of positive CRP and site of knee joint involvement.

Tabel 4: duration of knee OA associated to CRP

Result has shown, duration of most cases more than 1 year.

For duration less than 1 year (N=16), 10 of them have –ve CRP and 6 have +ve CRP. While for duration more than 1 year (N=27), 19 of them have –ve CRP and 8 have +ve CRP.

P value(0.006) so there is significant association between CRP and duration of knee OA.

Tabel 5: severity of knee OA associated to CRP

The results are shown 27 of total cases have sever pain at site of knee OA .

For mild knee OA(N=4), 2 of them have –ve CRP and 2 have +ve CRP. And for moderate knee OA (N=12), 10 of them have –ve CRP and 2 have +ve CRP. While sever knee OA (N=27), 17 of them have –ve CRP and 10 have +ve CRP.

P value(0.005) so there is significant association between CRP and severity of knee OA.

Table 6: presence of crepitus associated to CRP

The results are shown most cases have crepitus (N=32), 22 of them have –ve CRP and 10 have +ve CRP.

P value(0.036) this mean there is significant association between CRP and presence of crepitus.

Table 7: family history associated to CRP

The result showed there is no family history in both groups, cases and control(N=57) , 44 of them have –ve CRP and 13 have +ve CRP. While result which show threr is family history in both group , cases and control (N=18), 16 of them have –ve CRP and 2 have +ve CRP.

P value(0.279) so in our study show there is no significant association between CRP and family history.

Table 8: drug history associated to CRP

In both groups cases and control there is no drug history in (N=48), 39 of them have –ve CRP and have +ve CRP . Also for both groups cases and control there is family history in (N=27), 21 of them have –ve CRP and 6 have +ve CRP.

P value(0.718) so there is no significant association between CRP and drug history.

Table 9: BMI associated to CRP

The result has shown most of participants in our study was BMI ≥25kg/ m2.

For BMI <25 kg/m2 for both groups cases and control (N=27), 24 of them have –ve CRP and 3 have +ve CRP .

While, BMI≥25kg/ m2 for both groups case and control (N=48), 36 of them have –ve CRP and 12 have +ve CRP .

Pvalue(0.230) so there is no significant association beween CRP and BMI.

Table 10: x ray findings associated to CRP

Most cases in our study have one x ray finding (N=27), 21 of them have –ve CRP and 6 have +ve CRP.

For two x ray findings (N=14), 8 of them have –ve CRP and 6 have +ve CRP .

For three x ray findings (N=2) the 2 have +ve CRP .

Pvalue(0.001) so there is high significant association between CRP and x ray finding.

At the end of our study, the results showed that there is significant association between CRP and the data as age and bilateral site of knee OA for duration more than 1 year with severe pain and have crepitus with and x ray findings.

The results of this study are consistent with the results of previous studies

showing no associations between serum CRP levels and hip or knee OA . A population-based study among Europeans did not observe any associations of CRP levels, including no threshold effect, with the prevalence, incidence, or progression of radiographic hip or knee OA, after accounting for BMI . Another study among a European population did not observe any associations of CRP levels with risk of THR or TKR for OA, after adjusting for age, gender, BMI, and lifestyle factors . In contrast, a study among white and African American women observed that CRP levels were higher among those with incident knee OA and were strongest among obese women. however, findings were not adjusted for or stratified by race. A study among middle-aged to older white and African American adults observed no association between hs-CRP and incident radiological knee OA, osteophyte formation, or joint space narrowing .

Only one prior study examined the relationship between CRP GRS and OA. In this Mendelian randomization study among 5,755 knee OA cases and 18,505 controls, there was no association between the 4-SNP CRP GRS and risk of knee OA, but there was a 17% (HR, 1.17; 95% CI, 1.01–1.36) increased risk of knee OA per 1 mg/l increase in ln CRP for the 18-SNP polygenic GRS. However, this previous study did not examine hip OA; was exclusive to European populations; employed a case-control design; used summary- rather than individual-level data; and examined knee OA overall, without consideration of different OA phenotypes. Given that OA is a heterogeneous disease with many clinical phenotypes, it is necessary to distinguish different OA outcomes, such as early knee OA or end-stage knee OA as indicated by TKR.

In a study among white men and women from the Rotterdam Study, CRP haplotypes representing genetic variation in the *CRP* gene were not associated with the prevalence, incidence, or radiographic progression of hip or knee OA. These studies were conducted in white populations and did not examine racial and ethnic differences. Racial and ethnic minorities have not been adequately represented in studies examining GRS as predictors of adverse health outcomes. Due to heterogeneity in genetic architecture between individuals of varying ancestry, further studies of CRP GRS derived using significant genetic variants from ancestry-specific GWAS are currently needed to determine their utility in OA prediction.

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