

Prevalence of knee pain and its correlates with specific emphasis on CVD risk factors in Hisar urban population

Background: Literature shows osteoarthritis increases the cardiovascular disease related death. There are no such studies from Indian subcontinent that shows association between cardiovascular disease (CVD) risk factors and knee pain. Thus the aim of this study was to see the association between selected CVD risk factors and knee pain in urban Hisar population. **Methods:** Present study was a cross-sectional survey in which 1503 subjects (response rate 72.2%; female 54.2%) aged 30 years or more were randomly selected through multi-stage random technique. Data was collected through standardized questionnaire and published measurements techniques by two physiotherapists in summer 2016. Knee pain was defined as pain around knee joint that required meeting physician or physiotherapists or activity modification for at least 3 days in the last 12 months. Following variables were selected as CVD risk factors: age, sex, body mass index (BMI), waist circumference (WC), smoking habit, alcohol consumption, blood pressure (BP), fasting blood glucose (FBG). Standard cut-off values were used to define general obesity, abdominal obesity, hypertension, diabetes from BMI, WC, BP, FBG values respectively. Data was analysed using chi-square test and binary logistic regression technique. Results were presented as OR with 95% CI. All analysis were done using IBM-SPSS (21.0 version) software. **Findings:** Old age, female sex (OR 1.86; 95% CI 1.44-2.40), general obesity (1.94; 1.39-2.72), abdominal obesity (1.97; 1.42-2.75), non-smoking (1.48; 0.94-2.33), non-alcohol consumption (1.95; 1.17-3.26), hypertension (1.51; 1.18-1.94), diabetes (2.51; 1.83-3.45) were identified as risk factors for knee pain. After adjustment old age (1.06; 1.04-1.07), female sex (2.23; 1.69-2.96), general obesity (1.47; 1.01-2.13) and diabetes (1.65; 1.17-2.33) were identified correlates for knee pain in this urban population. **Limitation:** Results of this study are compared with osteoarthritis studies. **Conclusion:** There is conflicting (some positive and some negative) association between CVD risk factors and knee pain. Controlling weight, BP, FBG would reduce the knee pain.

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Introduction

Knee pain is more common in Indians than other ethnic groups with 6 months prevalence of 31.8% [1]. Chronic knee pain can potentially cause reduced work productivity through absenteeism [2]. Osteoarthritis (OA), worthy cause of knee pain, is an important public health issue-it has estimated to be a fourth leading cause of disability by 2020 [3]. Global ranking for OA, based on Years Lived with Disability (YLD), moved from 19th in 1990 to 13th in 2015 and OA is the 3rd leading musculoskeletal disorder for YLD [4].

Patient suffering from OA usually complains of pain and stiffness after work or standing for long time [5]. Assessing knee pain is an easy way to

screen OA knee instead of X-ray examination in large population studies as latter involve more cost and time [6]. Studies supports that knee pain is sensitive for OA knee with 70-80% people with knee pain have radiographic OA in middle and old age population [7-9].

Recent meta-analysis based on observational studies showed that there is association between OA and Cardiovascular Disease (CVD) related death with maximum risk in knee OA [10,11]. Old age, male sex, smoking, alcohol consumption, physical inactivity, obesity (both general and abdominal), elevated blood pressure (hypertension), elevated blood glucose (diabetes), elevated lipid profile (dyslipidemia) are some of the identified risk factors for CVD [12]. These factors are both positively or negatively associated

with OA and well documented in literature [13-15]. Literature are showing conflicting results between CVD risk factors (especially metabolic syndrome components) on OA knee depending on country in which the study was carried out [16-22].

Most of the current literature based on large population is mainly from developed countries and other Asian countries making difficult to understand the risk in India. Recent article from India based on large sample size reported the knee OA prevalence at 28.7%. But they did not report the odd ratio for different identified CVD risk factors [23].

The objectives of the present paper are to find out over-all, age specific, gender specific prevalence of knee pain in urban population of Haryana; to see the association between selected CVD risk factors and knee pain.

Methodology

Present study was a population based cross-sectional study conducted on urban geographical location (Hisar city, Haryana state, India-country). Selection sample, sampling technique were already published in our baseline data paper [24] with following modifications. Only five locations sample data has used- one location data was not available. Overall response rate was 72.20% (1540 out of 2133 invited subjects were agreed to participate). After removal of 37 subjects during validation phase, data of 1503 subjects (female 814-54.2%) were used in this paper. The mean \pm SD of age, height, weight, BMI of selected sample were 48.23 ± 13.12 years, 161.68 ± 8.46 cm, 67.96 ± 12.42 Kg, 25.97 ± 4.57 Kg m⁻² respectively.

Detailed data collection methods have been already published elsewhere [24]. Briefly, pre-designed questionnaire (in English), modified from pilot study done in 2015, and was administered to collect data. Following parameters, relevant to our objectives of this paper, were self-reported: age, height, weight, smoking, alcohol habits. The following parameters were measured and recorded in the questionnaire: BMI, Waist Circumference (WC), Blood Pressure (BP), and Fasting Blood Glucose (FBG).

Knee pain was defined as pain around knee joint that required meeting medical personnel (physician, physiotherapist) or pain that prevented from carrying normal ADL for at least 3 days in the past 12 months. Modified Nordic

musculoskeletal questionnaire (only middle 2 sections) with diagram used by de Barros and Alexandre [25], was used for this purpose.

BP was measured three times using automatic digital sphygmomanometer [OMRON[®], Binh Duong, Vietnam] in sitting position. SBP 130 mmHg or more and DBP 85 mmHg or more along with uncontrolled self-reported hypertension were classified as hypertension.

FBG was measured by hand-held portable glucometer [ACCU-CHECK Active, Mannheim, Germany]. FBG greater than 100 mg dL⁻¹ but less than 125 mg dL⁻¹ was classified as pre-diabetes. FBG greater than 125 mg dL⁻¹ or self-reported diabetes were classified as diabetes.

WC was measured using non-elastic inch at mid-way between 12th rib and anterior superior iliac spine. Measurement was recorded in the assessment form, questionnaire, to the nearest centimeter (cm) value. WC greater than 80-89 cm for females; 90-99 cm for males were classified as Asia specific abdominal obesity and 90 cm or more for females; 100 cm or more for males classified as abdominal obesity.

BMI was calculated from self-reported values of weight in kilogram and height in meters. The formula used was weight divided by height [2]. BMI <25 Kg m⁻², 25-29.99 Kg m⁻², 30 Kg m⁻² or more were classified as normal, overweight and general obesity respectively.

Over-all, sex and age stratified prevalence of knee pain was calculated in percentage. Chi-square test using cross-tabulation was used to see the association between variables and knee pain. If there was a significance in chi-square test variables were entered in to binary logistic regression individually as well as combination and enter method model was used for the presentation. All the analysis were done in IBM-SPSS (version 21.0).

Results

Table 1 shows prevalence rate according to selected variables along with missing values. One year prevalence of knee pain was 21.6%. Females (26.3%) were more complained than males (16.1%). It increased as age, BMI, WC increases. Smoking and alcohol consumption decreased the knee pain prevalence.

Table 2 shows association between 8 selected variables and one year knee pain in urban population using chi-square test (χ^2). Age,

Table 1. One year knee pain prevalence rate according to subcategories of selected variables along with missing values in urban population.

S. No.	Variables	Missing values (n)	Sub-category (n)	Prevalence rate (%)
1	Age	10	30-39 years (452)	09.10
			40-49 years (358)	17.00
			50-59 years (331)	22.70
			60 years or more (352)	41.80
2	Sex	00	Males (689)	16.10
			Females (814)	26.30
3	BMI	09	Upto 24.99 Kg m ⁻² (683)	18.30
			25-29.99 Kg m ⁻² (241)	22.10
			30 Kg m ⁻² or more (570)	30.30
4	WC	14	WC<80 cm (F); <90 cm (M) (358)	16.20
			WC 80-89 cm (F); 90-99 cm (M) (483)	17.40
			WC ≥ 90 cm (F); ≥ 100 cm (M)(648)	27.60
5	Smoking	00	Yes (smokers) (148)	16.20
			No (non-smokers) (1355)	22.20
6	Alcohol consumption	00	Yes (drinkers) (139)	12.90
			No (non-drinkers) (1364)	22.50
7	BP	00	No (normal BP) (874)	18.60
			Yes (hypertensives) (629)	25.80
8	FBG	12	No (normal) (913)	16.80
			Yes (Pre-diabetic) (334)	26.00
			Yes(Diabetic) (244)	33.60

BMI: Body Mass Index; WC: Waist Circumference; BP: Blood Pressure; FBG: Fasting Blood Glucose

Table 2. Association between knee pain and selected variables in urban population.

S. No.	Variables	df	Chi-Square (x ²) value	Sub Category	Unadjusted odd ratio (OR) (95% CI)
1	Age	3	30.56	30-39 years	Reference
				40-49 years	2.06 (1.35-3.14)
				50-59 years	2.94 (1.95-4.43)
				60 years or more	7.19 (4.89-10.56)
2	Sex	1	22.82	Male	Reference
				Females	1.86 (1.44-2.40)
3	BMI	2	15.17	Normal	Reference
				Overweight	1.27 (0.96-1.67)
				General obesity	1.94 (1.39-2.72)
4	WC	2	25.13	Normal	Reference
				Abdominal obesity (Asia)	1.09 (0.76-1.57)
				Abdominal obesity	1.97 (1.42-2.75)
5	Smoking	1	2.83	Yes	Reference
				No	1.48 (0.94-2.33)
6	Alcohol consumption	1	6.80	Yes	Reference
				No	1.95 (1.17-3.26)
7	BP	1	10.90	Normal	Reference
				Hypertension	1.51 (1.18-1.94)
8	FBG	2	37.32	Normal	Reference
				Pre-diabetes	1.75(1.30-2.36)
				Diabetes	2.51(1.83-3.45)

BMI: Body Mass Index; WC: Waist Circumference; BP: Blood Pressure; FBG: Fasting Blood Glucose

sex, WC, FBG (4 variables) were very highly associated with knee pain with significant $p < 0.001$. BMI, hypertension (2 variables) were the next significant variables associated with knee pain ($p = 0.001$). Alcohol consumption also associated with knee pain ($p = 0.009$). Smoking was not associated with knee pain ($p = 0.092$).

Prevalence of knee pain doubled in 40-49 years group; tripled in 50-59 years group and more than 7 times in 60 year or more group as compared to 30-39 years group. Females were 86% more risk for knee pain than male counterpart. General obesity and abdominal obesity doubled the risk of experiencing knee pain in one year. Smoking

and alcohol consumption prevented knee pain prevalence in this population. Non-smokers were 50% and non-drinkers were 100% more risk for knee pain. Individual with hypertension and diabetes were 50% and 150% more risk of experiencing knee pain.

Table 3 shows adjusted OR along with 95% CI when all 6/5 variables entered into binary logistic regression (multivariate). Enter method with constant was used for presentation. Age, sex, diabetes were significant and BMI was significant when WC was removed from the model. Being female more than doubled the risk of experiencing knee pain. Diabetes increased the knee pain prevalence by 50-65%. When age was entered as continuous variable instead of categorical in multivariate binary logistic regression along with other 5 categorical variables, OR (95% CI) for age was 1.055 (1.044-1.067).

Discussion

Overall one year self-reported knee pain prevalence is 21.6% in Hisar urban population. Old age, female sex, high BMI, high waist circumference, not smoking, not drinking alcohol, high blood pressure, high FBG are the possible risk factors for knee pain. After adjustment old age, female sex, and high FBG remained the correlates for knee pain in this population.

High FBG increase the knee pain risk by 50% (adjusted OR 1.53 for prediabetes and 1.65 for diabetes). Recent meta-analysis based on 49 studies, of which 28 were cross-sectional studies,

concluded that there is an association between diabetes and osteoarthritis (OR 1.51) [16]. Similar to majority of the studies, our result also shows this association is significant even after adjustment of BMI. However, there is no study from India that shows this relation. Diabetes has shown as risk factor for joint space narrowing-disease progression, in knee osteoarthritis [18]. Molecular mechanisms for OA in diabetes are given elsewhere [26], briefly, cartilage stiffness and permeability changes; biochemical changes in tendon; bone healing after micro fractures that are associated with diabetes among others [26].

Both overweight (OR 1.27; 95% CI 0.96-1.67) and obesity (OR 1.94; 95% CI 1.39-2.72) based on BMI increase the knee pain prevalence. However, this risk reduced to 1.47 (1.01-2.13) when the values are adjusted for age, sex, blood pressure, FBG values. This is supported by both Indian [23,27] as well as Asian/western studies [7-9,14,15,28,29]. The mechanism for knee pain in obese people is excessive load on weight-bearing joints due to excessive weight.

Abdominal obesity based on WC doubled the risk (OR 1.97; 95% CI 1.42-2.75) of one year knee pain prevalence. However, this was reduced to insignificant (OR 1.14; 95% CI 0.78-1.67) when the values were adjusted to age, sex, blood pressure and FBG level. There is no consensus on the association of central obesity and knee OA as some shows significant relation [19,21] on the other hand some shows relation is depends on gender [20,30].

Table 3. Adjusted odd ratio (OR) along with 95% confidence interval (95% CI) using multivariate binary logistic regression for selected variables.

S. No.	Variables	Sub-category	OR (95% CI)
1	Age	30-39	Reference
		40-49	1.84 (1.19-2.85)
		50-59	2.62 (1.70-4.03)
		60 or more	6.64 (4.41-9.98)
2	Sex	Males	Reference
		Females	2.23 (1.69-2.96)
3	BMI*	Normal	Reference
		General obesity	1.47 (1.01-2.13)
4	WC*	Normal	Reference
		Abdominal obesity	1.14 (0.78-1.67)
5	BP	No	Reference
		Yes	1.20 (0.91-1.59)
6	FBG	Normal	Reference
		Prediabetes	1.53 (1.11-2.11)
		Diabetes	1.65 (1.17-2.33)

BMI: Body Mass Index; WC: Waist Circumference; BP: Blood Pressure; FBG: Fasting Blood Glucose
*Denotes other variable removed from model i.e., BMI was without WC; vice-versa. Values were adjusted for other 5/4 variables

Hypertension increases (OR 1.51; 95% CI 1.18-1.94) the risk of knee pain prevalence in this population. But OR reduced to 1.20 (95% CI 0.91-1.59) when the values were adjusted for age, sex, BMI, FBG. Similar finding was observed in three Asian studies [19,29,31]. Morovic-Vergles *et al.* [17] concluded that the association between OA and hypertension is explained by age and BMI which is similar to our finding. However hypertension may affect the OA disease severity by arterial stiffness [32] and bone loss [33].

Both smoking and alcohol consumption shows protective effect on knee pain. This finding is new to India as there are no supporting findings from India. But several studies from outside India shows smoking act as protective role in knee pain [14,15]. Two Asian studies [29,31] found drinking act as protective role in knee pain. The exact mechanisms for these findings are not available and future studies should focus on this topic.

Age advancement increase the knee pain (adjusted OR 1.06; 95% 1.04-1.07). This means 6% rise in knee pain per year age raise starting from 30 years (risk is not linear). Similar risk has observed in Koreans [28] and rural Chinese [34]. Old age the risk factor for knee pain/OA is supported by several studies from India [23,27,35] and western literature [14,15].

Being female sex doubled the risk (adjusted OR 2.23; 95% CI 1.69-2.96) of knee pain. This is supported by both Indian [23,35] and Asian/western studies [1,7-9,14,15,28,29,31]. The possible mechanisms may be wider pelvis in females that results changes in femur and tibia alignment (deformity).

It is well known that age, sex, BMI are associated with knee pain. New findings emerged from this study are protective role of smoking and alcohol consumption as well as knee pain risk associated with hypertension and diabetes. These new findings are observed in other Asian/Western studies not from India.

Main limitation of this paper is that even though we have measured self-reported knee pain, we used knee OA studies (both cross-sectional and cohort) in the discussion to support our results. The rationale for this have been given in introduction i.e., OA is the most common condition that represents knee pain in middle and old age [7-9]. We have not classified the knee pain into acute or chronic which may be more reliable for OA than simple knee pain, but

we don't have the data to do this as the data was collected in early 2016. We assumed that OA is the cause of knee pain in our middle and old aged population hence we used OA literature.

The strength of this paper is that there is no study from India that focus the association between CVD risk factors and OA knee so far. Large sample studies on rheumatological conditions from India are rare. This study results will help to see the future trends in CVD risk factors and their association on knee pain.

CVD risk factors are having positive i.e., age, general and abdominal obesity, hypertension, diabetes as well as negative i.e., sex, smoking, and alcohol consumption association with knee pain. Majority of CVD are not significantly associated with knee pain after adjustment. Old age, female sex, BMI and diabetes are significant correlates for knee pain in this urban population aged 30 years or more.

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