

ASSOCIATION BETWEEN SERUM CARTILAGE OLIGOMERIC MATRIX PROTEIN LEVEL AND KNEE OSTEOARTHRITIS SEVERITY IN ELDERLY AT PUBLIC HEALTH CARE CLINICS UIN SYARIF HIDAYATULLAH JAKARTA IN 2017

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Abstract – Osteoarthritis is a chronic degenerative disease caused by degeneration of cartilage in the joints that increased friction between bones. Data from Riskesdas survey released by MoH RI 2013 reveals the prevalence of osteoarthritis (OA) at 24.7% while an independent study by Sonjaya (2016) shows that knee OA prevalence in Indonesia was about 45.58% between the age of 56-65. Serum cartilage oligomeric matrix protein (sCOMP) was proposed as a biomarker for OA severity. To identify the association between serum COMP level of knee OA patient and OA severity assessed by Kellgren-Lawrence radiological classification. This study used a cross-sectional design at KPKM Reni Jaya UIN SyarifHidayatullah Jakarta in February-Mei 2017 with a consecutive sampling. sCOMP level obtained from peripheral blood serum while radiographic imaging of the knee used for Kellgren-Lawrence evaluation. Respondent was given informed consent before enrolled in this study. Data were checked for variance and normality using boxplot, histogram, kurtosis, and skewness ratio before undergoing statistical analysis using RealStatsadd-in for Microsoft Excell 2016. Serum COMP level shows a significant association with age ($p=0.001$) and severity of OA ($p=0.01$). Analysis within the age subgroup of elderly shows that severity of OA was dependent on age with moderate effect size (0.24). A significant difference of serum COMP between mild and moderate severity of OA also present in the female, normal weight and advanced elderly (70-79) subgroups ($p<0.05$). Serum COMP level of OA patient significantly associated with a mild and moderate case of OA according to Kellgren-Lawrence classification.

INTRODUCTION

Osteoarthritis is “a long-term chronic disease involving the thinning of cartilage in joints which results in bone rubbing together, creating stiffness, pain and impaired movement” (Wittenauer, *et al.*, 2013). Basic health survey in 2013 reveals the prevalence of osteoarthritis (OA) in Indonesia at 24.7% (Kementerian Kesehatan, 2013). Knee OA among the participants of Framingham Osteoarthritis Study in age over 45 was 19.2% and 27.8% in the Johnston County Osteoarthritis Project. The third National Health and Nutrition Examination Survey (NHANES III) reveals 37% participant in age over 60 had radiographic knee OA (KOA) (Zhang and Jordan, 2010). Sonjaya, (2016)

study in Al-Islam Hospital, Bandung shows a prevalence of 45.58% primary KOA between the age of 56-65 and 40.04% between the age of 66-75 (Sonjaya, 2016).

Knee OA affect the medial, lateral and patellofemoral joint which develops over the course of 10-15 years and considered as a multifactorial in origin. The radiologic evaluation may be used to make a diagnosis of KOA with the most frequent radiographic grading system is described by Kellgren and Lawrence (Lespasio, *et al.*, 2017). Briefly, The Kellgren-Lawrence Classification of Osteoarthritis was assigned for each radiograph a grade from 0 to 4. Grade 0 signifying no presence of OA and Grade 4 signifying severe OA (Kohn, *et al.*, 2016).

Recently, a systematic review and meta-analysis study by Hoch *et al.* concluded that serum cartilage oligomeric matrix protein elevated in KOA patients and sensitive to OA disease progression. This study suggested that studies need to be conducted to investigate the use of sCOMP as a biomarker for OA development and progression (Hoch *et al.*, 2011). Singh *et al.*, (2014) recommended sCOMP levels can be used to diagnose normal and diseased individual and also assess different grade of severity of KOA. (MISSING: shahi 2013 comparison, 2018) Verma *et al.* added that sCOMP could also have a prognostic value in determining the patients at risk of rapidly progressing this debilitating disease (Verma and Dalal, 2013). This study aims to identify the association between serum COMP level of knee OA patient and OA severity assessed by Kellgren-Lawrence radiological classification in the elderly population at Public Health Care Clinic of Reni Jaya UIN Syarif Hidayatullah Jakarta in 2017.

MATERIALS AND METHODS

This study is an analytical cross-sectional study with symptomatic KOA patient as the study subject. The subjects were invited to the study in January 2017, given informed consent and recruited from Rural Public Health Care Clinic of Jakarta Islamic State University using a consecutive sampling method. All recruited subjects over 60 years old, BMI below 27 kg/m², with symptomatic KOA, without prior heavy physical activity the previous month, history of knee trauma, other systemic inflammation diseases, undergone arthroplasty, arthrodesis and osteotomy subsequently undergone physical examination, serum COMP measurement and knee

radiologic examination. 147 patients agreed to join the study and completed all examinations.

Blood samples collected from all subjects for sCOMP measurement in a clinical laboratory (Prodia). Radiologic examination conducted at Sari Asih Hospital and interpreted by an orthopedist and classified using the Kellgren-Lawrence classification. All measurement data collected and analyzed using Microsoft Excell add-in for statistical analysis (Real Stat) available for download at <http://www.real-statistics.com/free-download/>. Data checked for normality using boxplot, histogram, kurtosis and skewness ratio. Data analyzed by t-test or Mann-Whitney for two independent samples to identify the statistical difference in numerical variables and chi-square test for categorical variables. Proposed sCOMP cut-off point by Singh *et al.* Normal (up to 652.5 ng/mL), Mild KOA (up to 801.5 ng/mL), Moderate KOA (up to 1100.5 ng/mL) and Severe KOA (over 1100.5 ng/mL) used to against our Kellgren-Lawrence grading and sCOMP data. Significance less than 5% were considered significant.

RESULTS AND DISCUSSION

This study revealed that the majority of osteoarthritis patient in the public health care clinic of Reni Jaya UIN Syarif Hidayatullah, Jakarta was female (72.8%) during the time of the study (Table 1). Most of the respondent in this study have normal to overweight body mass index (85.7%) with an age range at 60-69 years old (73.5%) and a mild-moderate severity according to Kellgren-Lawrence (82.2%). Analysis of subgroup shows that KOA severity is equal between gender and body mass

Table 1. KOA Patient Characteristic

Parameter		% (count)	COMP ng/mL (SE/min-max)*
Sex	Male	27.2 (40)	772.2 (355.3-1870) ^a
	Female	72.8 (107)	737.4 (358.5-2160) ^a
BMI	<17	1.4 (2)	768.6 (639-898.3) ^a
	17-18,4	4.8 (7)	775.8 (149.5) ^a
	18,5-25	59.2 (87)	730.7 (355-2160) ^a
	25,1-27	34.7 (51)	769.5 (376.7-1870) ^a
Age	60-69	73.5 (108)	703.2 (355.3-2160) ^a
	70-79	26.5 (39)	867.6 (359-1870) ^b
OA Severity (Kellgren)	Mild	42.8 (63)	685.9 (355.3-2160) ^a
	Moderate	39.4 (58)	771.1 (358.5-1254.5) ^b
	Severe	17.7 (26)	840.3 (464.8-1870) ^b

*difference in notations (a,b) shows a significant difference (p<0.05) with t-test or Mann-Whitney for two independent samples

index ($p > 0.05$) but significantly different between age group ($p < 0.05$) (Table 2).

There was also a significant difference of mean serum COMP value between age group which shows that increase in age of respondent correlates with the increase of serum COMP value and KOA severity by Kellgren-Lawrence. However, a significant difference of mean serum COMP value only detected between mild and moderate-severe KOA severity (Table 1). Singh *et al.* (2014) proposed a sCOMP cut of point value to determined OA severity that we tested on our data. The analysis shows a substantial proportion (42.2%) of our respondent will be classified as normal based solely on the proposed sCOMP cut of value (Table 3). The remaining respondent with mild severity by Kellgren-Lawrence shows a mean sCOMP value that higher than proposed cut of point and lower for those which classified as moderate and severe by Kellgren-Lawrence.

Our data show that serum COMP value significantly increased with age with a moderate

effect size but unable to differentiate between moderate and severe KOA classified by Kellgren-Lawrence. However, serum COMP level differs significantly between mild and moderate-severe cases. These results suggest that serum COMP level was more useful as a prognostic indicator for disease progression by Verma *et al.* instead of Singh *et al.* that proposed sCOMP for diagnosis and severity grading (Singh *et al.*, 2014; Verma and Dalal, 2013). Patient with mild OA severity and advanced age will benefit from sCOMP monitor to predict disease progression.

CONCLUSION

This study concluded that sCOMP level significantly associated with a mild KOA severity of female in advanced elderly age group.

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Table 2. KOA Severity in Patient Subgroup

Parameter	OA Severity (Kellgren-Lawrence)*			p value**	
	Mild	Moderate	Severe		
Sex % (count)	Male	47.5 (19)	35 (14)	17.5 (7)	>0.05
	sCOMP	693.1 (355.3-1559) ^a	790.9 (57.5) ^a	949.1 (182.4) ^a	
	Female	41.1 (44)	41.1 (44)	17.7 (19)	>0.05
	sCOMP	682.7 (369-2160) ^a	764.9 (358.5-1613) ^b	800.2 (518.7-1613) ^b	
BMI % (count)	<17	50 (1)	-	50 (1)	>0.05
	17-18,4	71.4 (5)	28.6 (2)	-	
	18,5-25	43.7 (38)	40.2 (35)	16.1 (14)	
	sCOMP	686.6 (355.3-2160) ^a	774.5 (42.6) ^b	734.8 (58.9) ^{ab}	
	25,1-27	37.2 (19)	41.1 (21)	21.6 (11)	
Age % (count)	sCOMP	631.2 (38.6) ^a	777.6 (420.4-1192.6) ^b	992.9 (567-1807) ^b	<0.05 (effect size 0.2)
	60-69	49.1 (53)	38 (41)	12.9 (14)	
	sCOMP	684.4 (355.3-2160) ^a	700.3 (358.5-1613) ^{ab}	783.1 (58.6) ^b	
	70-79	25.6 (10)	43.6 (17)	30.8 (12)	
	sCOMP	693.9 (359-1559) ^a	941.9 (56.3) ^b	907.1 (541-1870) ^{ab}	

*difference in notations (a,b) shows a significant difference ($p < 0.05$) with t-test or Mann-Whitney for two independent samples, same notations shows no significant difference (ab with a and b). sCOMP in ng/mL (standard error or min-max). ** chi-square test for independence

Table 3. Evaluation of Proposed sCOMP Cut Off Point by Singh *et al.* [6]

KOA Severity	COMP cut off point	%(count)	sCOMP ng/mL (SE/min-max)*
Normal (No-OA)	652.5	42.2 (62)	-
Mild	801.5	25.2 (37)	899.7 (661-2160) ^a
Moderate	1100.5	23.8 (35)	916.1 (660-1382) ^a
Severe	Over 1100.5	8.8 (13)	964.1 (660.9-1870) ^a

*COMP value of patient above 652.5 which classified using Kellgren for OA severity, the difference in notations (a,b) shows a significant difference ($p < 0.05$) with t-test or Mann-Whitney for two independent samples

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