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AB1293 SMAD3 GENE POLYMORPHISMS AND EXPRESSION IN SERUM AND CARTILAGE INFLUENCE THE RISK OF KNEE OSTEOARTHRITIS

Rajeswar Nath Srivastava, Amar Chandra Sharma, Sudeepti Srivastava, Saloni Raj. *King George's Medical University, orthopaedic surgery, Lucknow, India*

Background: Knee Osteoarthritis (KOA) is the most common degenerative arthritis, a type of arthritis that is caused by breakdown of articular cartilage with eventual loss of the cartilage of the joints. Smad3 is a key intracellular messenger in the transforming growth factor β signaling pathway. Previous study suggested Smad3 gene mutation is a possible predisposing factor for human OA and found gene mutation in OA, providing insight into the function of SMAD3 mediated TGF- β signals in the development of OA and also suggested that Smad3 gene mutation may be a risk factor for genetic susceptibilities to OA. In this case control study, we investigated the possible correlation between the SNPs Smal (C/T; rs6494629), FokI (A/C; rs2289263) in Smad3 gene and susceptibility to knee OA and validated in serum and cartilage.

Objectives: To investigate the possible association between SNPs (rs6494629 and rs2289263) of the Smad3 gene and KOA.

Methods: In this study cases consisted of men and women ≥ 40 years that fulfilled American College of Rheumatology (ACR) clinical and radiographic criteria for knee OA. Venous blood samples were obtained from all cases as well as controls for genetic analysis. Polymerase chain reactions were performed for SNP analysis using specific primer. Total protein was measured in serum by an enzyme linked immunosorbent assay according to the manufacturer's Protocol (ELISA) and in cartilage tissue done by western blot.

Results: A total of 200 cases that confirmed radiographic knee OA and equal number of age and sex matched healthy controls were enrolled. There was no significant difference in demographic characteristics between the cases and controls. A SNP (rs6494629 and rs2289263) mapping to intron 1 of SMAD3 was associated with knee OA ($P < 0.013$ and $P < 0.044$, respectively). Within the SNPs (rs6494629) of Smad3 gene, genotype CC and CT was found to be significantly ($p < 0.013$) associated with knee OA as compared with the CC genotype and SNP rs2289263, genotype CC and CA was found to be significantly ($p < 0.044$) associated with knee OA as compared with the AA genotype. In addition when alleles were compared, C allele of both the studied SNP was observed to be significantly associated with knee OA. Serum levels of Smad3 in KOA patients with rs6494629 TT, CT and CC genotypes were significantly higher than healthy subjects with the same rs6494629C/T genotypes (all $P < 0.0001$, $P < 0.0006$, $P < 0.017$ respectively). Increased serum levels of Smad3 were also observed in KOA patients with rs2289263 AA, CA and CC genotypes compared to controls (all $P < 0.006$, $P < 0.0006$, $P < 0.004$). We performed Immunoblot analysis on cartilage tissue from 15 cases and 10 controls. The smad3 level in cases was significantly higher than controls ($P < 0.006$).

Conclusion: Our data indicate that genetic variation in the SMAD3 gene is involved in the risk of knee OA in North Indian populations, confirming the results from previous studies on the potential importance of this gene in the pathogenesis of OA. Further we also validated these genetic variations at protein level in both blood and tissue and found significant association.

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AB1294

IMPACT OF INFERTILITY, PREGNANCY LOSS AND CHILDBEARING DECISION ON FAMILY SIZE IN WOMEN WITH SYSTEMIC LUPUS ERYTHEMATOSUS AND RHEUMATOID ARTHRITIS

Dayang Masyrinartie Suahilal¹, Nurulraziqin Mohd Jamid¹, Noraini Mat Husin², Hairul Hadi Ariff¹, Rashidah Bahari³, Nor Shuhaila Shahril¹. ¹Hospital Putrajaya, Medicine, Putrajaya, Malaysia; ²Hospital Raja Permaisuri Bainun, Ipoh, Medicine, Ipoh, Malaysia; ³Hospital Putrajaya, Clinical Research Centre, Putrajaya, Malaysia

Background: Systemic lupus erythematosus (SLE) and Rheumatoid Arthritis (RA) often affects women in their reproductive years. These women are faced with a life-long illness that may have considerable impact not only on their physical health, but also on their reproductive potential. Fertility of these women may also be affected by the disease, treatment and/or organ damage.

Objectives: To determine the role of infertility, pregnancy loss and childbearing decision and patients concerns on family size in women with SLE and RA

Methods: A cross sectional study using a self-administered reproductive history questionnaire completed by woman with SLE/RA attending Rheumatology clinic follow up in Hospital Putrajaya, Hospital Tengku Ampuan Rahimah, and Hospital Raja Permaisuri Bainun, Malaysia from 1 January 2017 to 30 June 2017.

Within each disease cohort, women were identified into 3 groups, those with fewer children than planned (group A), those with same number of planned children (group B) and those with completed family or not interested in having any children (group C). Data on number of children, pregnancies, miscarriages and self reported infertility were recorded. For group A, data on patient concerns and the factors that could impact family building were also obtained.

Results: Total of 110 women with SLE and 91 women with RA were surveyed. The mean age of women with SLE and RA were 37.6 years ($\pm$ SD 7.4) and 45.37 years ($\pm$ SD 11.7) respectively. Majority of women (48.8%) with SLE and RA were in group A with 59% ($n=65$) of women with SLE and 33% ($n=33$) of women with RA had fewer children than originally planned.

The average numbers of pregnancies were similar in both cohorts, but women with SLE had 1 less child and were more likely to report infertility and had higher rate of miscarriages (Table 1). SLE group A had a similar number of pregnancies, but 1 less child compared to SLE group B and C (Table 2). Similarly, among women with RA, group A had 1 less child with similar number pregnancies and miscarriage rate (Table 2). In both groups of women, concerns about inability to care for a child, damage from medications, and genetic transmission of their disease were associated with a lower pregnancy rate.

Table 1. Number of pregnancies, live births, miscarriages and rate of infertility among women with SLE and RA*

	SLE	RA	P
No. of pregnancies	2.28 ± 1.626	2.60 ± 1.949	0.128
No. of children	1.85 ± 1.235	2.19 ± 1.731	0.019
No. of miscarriages	0.46 ± 0.809	0.36 ± 0.659	0.040
No reporting infertility (%)	5 (4.5)	2 (2.2)	0.366

*values are the mean $\pm$ SD unless otherwise indicated

Table 2. Pregnancy outcomes for women with SLE ($n=110$) and RA ($n=91$) *

	Fewer children than desired (group A)		Expected number of children (group B)		completed family (group C)	
	SLE	RA	SLE	RA	SLE	RA
No. of woman, n (%)	65 (59.1)	33 (36.3)	20 (18.2)	31 (34.1)	25 (22.7)	27 (29.7)
No. of pregnancies	2.11 $\pm$ 1.592	2.03 $\pm$ 1.723	2.3 $\pm$ 0.865	2.81 $\pm$ 2.12	2.72 $\pm$ 2.092	3.07 $\pm$ 1.9
No. of children	1.57 $\pm$ 1.212	1.55 $\pm$ 1.416	2.1 $\pm$ 0.553	2.39 $\pm$ 4.856	2.36 $\pm$ 1.497	2.74 $\pm$ 1.745
No. of miscarriages	0.51 $\pm$ 0.831	0.36 $\pm$ 0.603	0.25 $\pm$ 0.716	0.32 $\pm$ 0.653	0.52 $\pm$ 0.823	0.41 $\pm$ 0.747

*values are the mean $\pm$ SD unless otherwise indicated

Conclusion: In this population, more than half of women with RA or SLE had fewer children than desired. Other than patient choice, infertility and miscarriage also play an important role on family size.