ResearchArticle Mishra & Agnihotry, 9(5&6): May-June, 2018:5810-5812]
CODEN (USA): IJPLCP ISSN: 0976-7126

INTERNATIONAL JOURNAL OF PHARMACY & LIFE SCIENCES
(Int. J. of Pharm. Life Sci.)

# Association of PPARG2 pro12ala polymorphism with osteoarthritis in Central India

**Alpana Mishra[1]* and Santosh Agnihotry[2]**
1, Centre for Biotechnology Studies, APS University, Rewa, (M.P.) - India
2, Dept. of Botany, Govt. Science College, Rewa, (M.P.) - India

## Abstract

The aim of this study was to investigate the possible association between the Pro12Ala polymorphism of the PPARγ gene with osteoarthritis in vindhya region population. We performed PCR-restriction fragment length polymorphism to determine the Pro12Ala polymorphism in 140 patients with osteoarthritis and 160 normal control subjects. Distribution pattern of genotypes and allele frequency suggests no significant difference among case and control group. PPARG2 polymorphism is not associated with risk of osteoarthritis in this region.

**Keywords:** Polymorphism, Frequency, Gene

## Introduction

Osteoarthritis (OA) is a group of distinct but over lapping diseases, often with different etiologies, but with similar biological, morphological and clinical manifestations. The disease process not only affects the articular cartilage, but also involves the entire joint, including the subchondral bone, ligaments, capsule, synovial membrane and periarticular muscles. Ultimately, the articular cartilage disintegrates with the onset of fibrillation, fissures, ulceration and formation of deep clefts. Osteoarthritis (OA) is a complex disorder with genetic and environmental risk factors both contributing to its development and progression (Felson et al. 2000). Obesity is one of the strongest environmental risk factors for knee OA (Blagojevic et al. 2010) and is considered to be moderately associated with hip OA (Lievense et al. 2002; Spector and MacGregor 2004). Several chromosomal loci and gene variations have also been reported to influence OA disease processes (Ryder et al. 2008).

Osteoarthritis is the single most common cause of disability in older adults. The 2010 Global Burden of Disease Study reports that the burden of musculoskeletal disorders is much larger than estimated in previous assessments and accounts for 6.8% of DALYs worldwide (Laupattarakasem W et al,2008). An estimated 10% to 15% of all adults aged over 60 have some degree of OA, with prevalence higher among women than men (Lancet,.2012).

* Corresponding Author
E.mail: arpnna10mishra@gmail.com

PPARγ is a ligand-activated transcription factor and member of the nuclear receptor superfamily. Agonists of PPARγ inhibit inflammation and reduce synthesis of cartilage degradation products both in vitro and in vivo, and reduce the development/progression of cartilage lesions in OA animal modelsPeroxisome proliferator-activated receptors (PPARs) are ligand-activated transcription factors belonging to the nuclear hormone receptor superfamily (5). There are three isoforms, encoded by separate genes: PPAR-[gamma], PPAR-[alpha], and PPAR-[beta]/[delta] ,which share 60% to 80% homology in their ligand-and DNA-binding domains, and exhibits distinct patterns of expression and overlapping and distinct biological activities (Forman BM et al., 1997).

## Material and Methods

Study population

The study population consisted of 400 unrelated subjects and comprised 190 T2D patients and 210 ethnically matched healthy controls of Indo-European ethnicity. Cases included consecutive patients who attended the Department of Medicine at Shyam Shah Medical College, Rewa, India; Ayurveda Medical College, Rewa, India; Ranbaxy Pathology Regional Collection Centre, Rewa, India; and the District Hospital, Satna, India.

**DNA isolation**

Genomic DNA was extracted from whole blood using a modified version of the salting-out procedure described by Miller et al.

**Detection of ENPP1 and PPARG2**

single-nucleotide polymorphisms using polymerase chain reaction (PCR) restriction fragment length

polymorphism The P12A (substitution of A base to C at 12 exon) polymorphism of the PPARG2 gene was amplified by PCR. The oligonucleotide sequences (primers; see following) were designed to amplify the wild-type gene but lacked a restriction site for the BstU1 enzyme; however, as the alanine allele contains a restriction site, it cleaved to the 227 and 43 base pair (bp) fragments. (Hara et al.,2000)
Forward primer: 5′-GCCAATTCAAGCCCAGTC-3′.
Reverse primer: 5′GATATGTTTGCAGACAGTGTAT-CAGTGAAGGAATCGCTTTCCG3′.

## Results and Discussion

Overall genotype pattern of PPAR-γ gene polymorphism Pro12Ala was not significantly different between case and control ($\chi 2$ =1.815, P value=0.4036). Osteoarthritis group showed decrease in 'AA' genotype as compared to control group (67.9 % vs 72.5%) but statistically was not significantly different. Genotype 'GG' was non-significantly higher in HC group as compared to OA group (4.2% vs. 1.9%). An odds ratio of 2.343 for 'GG' genotype indicated a protective effect of this less common genotype in our population. An odds ratio of 0.8008 of common 'AA' genotype group respectively was consistent with little or no effect of this genotype in OA susceptibility. The heterozygous genotype 'AG' was non-significantly distributed in HC group as compared to OA group (27.9% vs 25.6%). An odds ratio of 1.121of 'AG' showed weak protective or no association in OA susceptibility.
Overall allele distribution was also nonsignificant but less common 'G' allele was found in higher frequency in control as compare to OA patients (14.7% vs 18.3%) and A allele was found at higher frequency in case as compare to control (81.7% vs 85.3%) but the difference was not significant ($\chi 2$ =1.359P=0.2437). Carriage rate of allele 'A' was equivalent to HC group and OA group. Whereas carriage rate of allele 'G' was lower in control group (32.1 % vs. 27.5%) but not significantly different between case and control ($\chi 2$=0.5573, P=0.4554). odds ratio of minor allele 'G' was 1.198 which clearly indicates its little or moderate protective effect of minor allele "G" in our population meanwhile odds ratio of 0.8345 for Major allele 'A' showed its little association with RA susceptibility but overall lack of significance was seen.

The pattern of genotype and allele distribution in disease and control group suggested lack of association of PPAR-γ in OA susceptibility. We studied the prevalence of the PPAR-γPro12Ala (rs1801282) missense mutation which has been shown to be associated with metabolic disorders such as type 2 diabetes (Tripathi AK et al. 2013), obesity (Galbete et al. 2013) and essential hypertension (Gu et al. 2013). However, in the current study we did not find a significant association between the PPARγ Pro12Ala missense mutation and knee OA in a Indian population. The Pro12Ala polymorphism has been associated with improved insulin sensitivity [. Ek J, 2001], reduced risk of type 2 diabetes [Ridker PM, 2004], myocardial infarction [Ridker PM, 2003], and atherosclerosis [Temelkova-Kurktschiev T, 2004]. This is consistent with a previous study by Al-Jarallah et al. (2011) in a Kuwaiti population.

**Table 1: pro12ala(rs1801282)genotypes, alleles and carriage rates with susceptibility to disease (osteoarthritis) cases compared to HC population in Central India.**

| VDR GENOTYPE | CASE N= 140 | | CONTROL N=160 | | $\chi^2$ VALUE (*P* VALUE) |
|---|---|---|---|---|---|
| | N | % | N | % | |
| AA | 95 | 67.9 | 116 | 72.5 | 2.266, (0.3383) |
| AG | 39 | 27.9 | 41 | 25.6 | |
| GG | 6 | 4.2 | 03 | 1.9 | |
| **ALLELES** | | | | | |
| A | 229 | 81.7 | 273 | 85.3 | 1.773, (0.1318) |
| G | 51 | 18.3 | 47 | 14.7 | |

| | | | | | |
|---|---|---|---|---|---|
| **CARRIGE RATE** | | | | | |
| A | 134 | 91.8 | 157 | 98.1 | 0.7447, (0.3882) |
| G | 45 | 32.1 | 44 | 27.5 | |

N - Number of individuals carrying particular genotype in a study group
% - Genotype frequency, allele frequency and carriage rates in percentage;
*- significant values
$\chi^2$ (*P* Value) - indicates $\chi^2$ *P* Value when HC is compared to OA

## References

1. Al-Jarallah K. F., Shehab D. K. and Haider M. Z. 2011 Prevalence of the Pro12Ala missense mutation in the PPARG2 gene in Kuwaiti patients with primary knee osteoarthritis. Ann. Saudi. Med. 31, 35–39
2. Arvind kumar Tripathi**,** Smriti Shukla, Mrigendra Kumar Dwivedi, Jitendra Kumar Tripathi, U. K. Chauhan, Shivam Singh, Manoj Indurkar (2013) "Type 2 diabetes in a central Indian population: association with PPARG2 P121A allele but not ENPP1 K121Q." Advances in Genomics and Genetics 2013:3 1–9
3. Blagojevic M., Jinks C., Jeffery A. and Jordan K. P. 2010 Risk factors for onset of osteoarthritis of the knee in older adults: a systematic review and meta-analysis. Osteoarthr. Cartilage 18, 24– 33.
4. Felson D. T., Lawrence R. C., Dieppe P. A., Hirsch R., Helmick C. G., Jordan J. M. et al. 2000 Osteoarthritis: new insights. Part 1: the disease and its risk factors. Ann. Intern. Med. 133, 635–646.
5. Galbete C., Toledo E., Martinez-Gonzalez M. A., Martinez J. A., Guillen-Grima F. and Marti A. 2013 Pro12Ala variant of the PPARG2 gene increases body mass index: An updated metaanalysis encompassing 49,092 subjects. Obesity (Silver Spring) 21, 1486–1495.
6. Gu S. J., Liu M. M. and Guo Z. R. 2012 Gene-gene interactions among the peroxisome proliferator-activated receptor polymorphisms for hypertriglyceridemia. Zhonghua Yu Fang Yi Xue Za Zhi 10, 916–921.
7. Hara K, Okada T, Tobe K, et al. The Pro12Ala polymorphism in PPAR gamma2 may confer resistance to type 2 diabetes. Biochem Biophys Res Commun. 2000;271(1):212–216.
8. Lievense A. M., Beerma-Zeirstra S. M., Verhagen A. P., van Baar M. E., Verhaar J. A. and Koes B. W. 2002 Influence of obesity on the development of osteoarthritis of the hip: a systematic review. Rheumatology 41, 1155–1162.
9. Miller SA, Dykes DD, Polesky HF. A simple salting out procedure for extracting DNA from human nucleated cells. Nucleic Acids Res. 1998; 16(3):1215.
10. Ryder J. J., Garrison K., Song F., Hooper L., Skinner J., Loke Y. et al. 2008 Genetic associations in peripheral joint osteoarthritis and spinal degenerative disease: a systematic review. Ann. Rheum. Dis. 67, 584–591.
11. Spector T. D. and MacGregor A. J. 2004 Risk factors for osteoarthritis: genetics. Osteoarthr. Cartilage 12, S39—44.

**How to cite this article**
Mishra A. and Agnihotry S. (2018). Association of PPARG2 pro12ala polymorphism with osteoarthritis in Central India. *Int. J. Pharm. Life Sci*., 9(5&6):5810-5812.
Source of Support: Nil; Conflict of Interest: None declared

**Received: 22.04.18; Revised: 20.05.18; Accepted: 29.05.18**