

(FC-04)

## Investigation of Association Between Paraoxonase-1 L55M (RS854560) and Q192R (RS662) Polymorphisms and Potential Atherosclerotic Risk Factors in PCOS Patients

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The aim of this study was to examine the frequency of potential atherosclerotic risk markers Q192R (rs662) and L55M (rs854560) in patients with PCOS and control group in Turkish women.

Blood samples were collected from 151 patients with PCOS and 52 healthy women at Recep Tayyip Erdoğan University Hospital, Rize. All individuals underwent an evaluation of clinical examination and transabdominal ultrasound. Genomic DNA was extracted from the samples. RFLP method was performed following the amplifications of the target regions. The L55M and Q192R polymorphisms were detected by AlwI and NlaIII digestion, respectively. The genotyping results of 88 samples of this cohort were also confirmed by DNA sequencing.

Patients with 192QR/192RR genotypes had a 2.5-time higher risk of representing PCOS compared to the individuals with 192QQ genotype. Differences in genotype and allele frequencies of PON1-55 were not found to be significant. Q192R (AUC: 0.613,  $p=0.017$ ) and BMI (0.618,  $p=0.012$ ) were established to be significant predictors of PCOS in a model including fasting glucose, insulin, HOMA-IR, total cholesterol, triglyceride, and LDL/HDL ratio as covariates (AUC: 0.655,  $p=0.001$ ). Q192R was more strongly correlated with PCOS than previously suggested atherosclerotic risk factors, BMI, metabolic syndrome (MetS), and insulin resistance (IR).

Q192R discriminates the patients with PCOS from controls significantly. Although further studies are needed, we suggest that individuals carrying an R allele are at a higher risk of developing PCOS in Turkish women. Q192R may be suggested to be a surrogate and robust predictive marker for the risk of developing PCOS and atherosclerosis in individuals.

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## Hyperandrogenism and Skeletal Dysplasia: Evaluation of 7 Patients with *PAPSS2* Gene Mutation

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The synthesis of PAPS (3-phosphoadenosine 5-phosphosulfate) - a sulfate donor - is catalyzed by two isoenzymes (PAPS synthase 1 and PAPS synthase 2). *PAPSS1* is ubiquitously expressed in human tissues, including cartilage. *PAPSS2* shows a restricted expression pattern and is the major isoform involved in cartilage growth. *PAPSS2* is responsible from the sulfation of dehydroepiandrosterone (DHEA) which is an androgen precursor. Impaired sulfation of DHEA leads to increase in the levels of active androgens and clinical findings of hyperandrogenism occurs. Homozygous mutations in the *PAPSS2* gene lead to impaired sulfation of proteoglycans and cause spondyloepimetaphyseal dysplasia (SEMD) Pakistani type which is characterized by short stature, short bowed legs, platyspondyly, narrow intervertebral spaces, short femoral neck, irregular metaphyses, and epiphyses. The aim of this study was to describe the molecular, clinical, and endocrinological features of patients diagnosed with SEMD Pakistani type.

Seven patients from three families were evaluated. 5 patients from the first family (16y/M-33y/F-38y/F-34y/M-14y/M) had short stature (-5 SDS/-6 SDS/-6 SDS/-3.7 SDS/-2 SDS, respectively). A 33-year-old female patient had oligomenorrhea, hirsutism, and mildly elevated testosterone level after puberty and a 38-year-old female patient had infertility for 5 years. A 7-year-old girl from the second family suffered from back pain and short stature (-2SDS) and a 15-year-old girl from the third family had scoliosis and short stature (-5.45SDS).

All cases were clinically and radiologically compatible with SEMD Pakistani type. Plasma level of DHEAS was low in all patients. Homozygous c.1000C > T mutation was found in patients from the first and third families and compound heterozygote novel pathogenic c.639 + 1G > T and c.1000C > T mutations were found in a patient from the second family.

In conclusion, endocrinologic problems can be seen in patients with SEMD Pakistani type and patients should be monitored for these disorders.