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# Longer trinucleotide repeats of androgen Receptor Gene: Infertility in males

Mussarat Ashraf
*Aga Khan University*, mussarat.ashraf@aku.edu

Hemaila Tariq
*Aga Khan University*

Rehana Rehman
*Aga Khan University*, rehana.rehman@aku.edu

# Longer trinucleotide repeats of androgen Receptor Gene: Infertility in males

Mussarat Ashraf,[1] Hemaila Tariq,[2] Rehana Rehman[3]

Madam, male infertility affects 15% of couples which is equivalent to 48.5 million couples globally.[1] Genetic tests for the diagnosis of cause of infertility have been used to develop guide lines to inform risk of transmission of genetic characteristics while electing for assisted reproduction.[2] Study done by Atif et al documented that routine screening for Y chromosome microdeletion is important for proper genetic counseling because this can presumably be transmitted as a fertility problem to their sons.[3] It is, therefore, very important to offer proper genetic counseling to the infertile couples particularly those who wish to undergo assisted reproductive techniques.

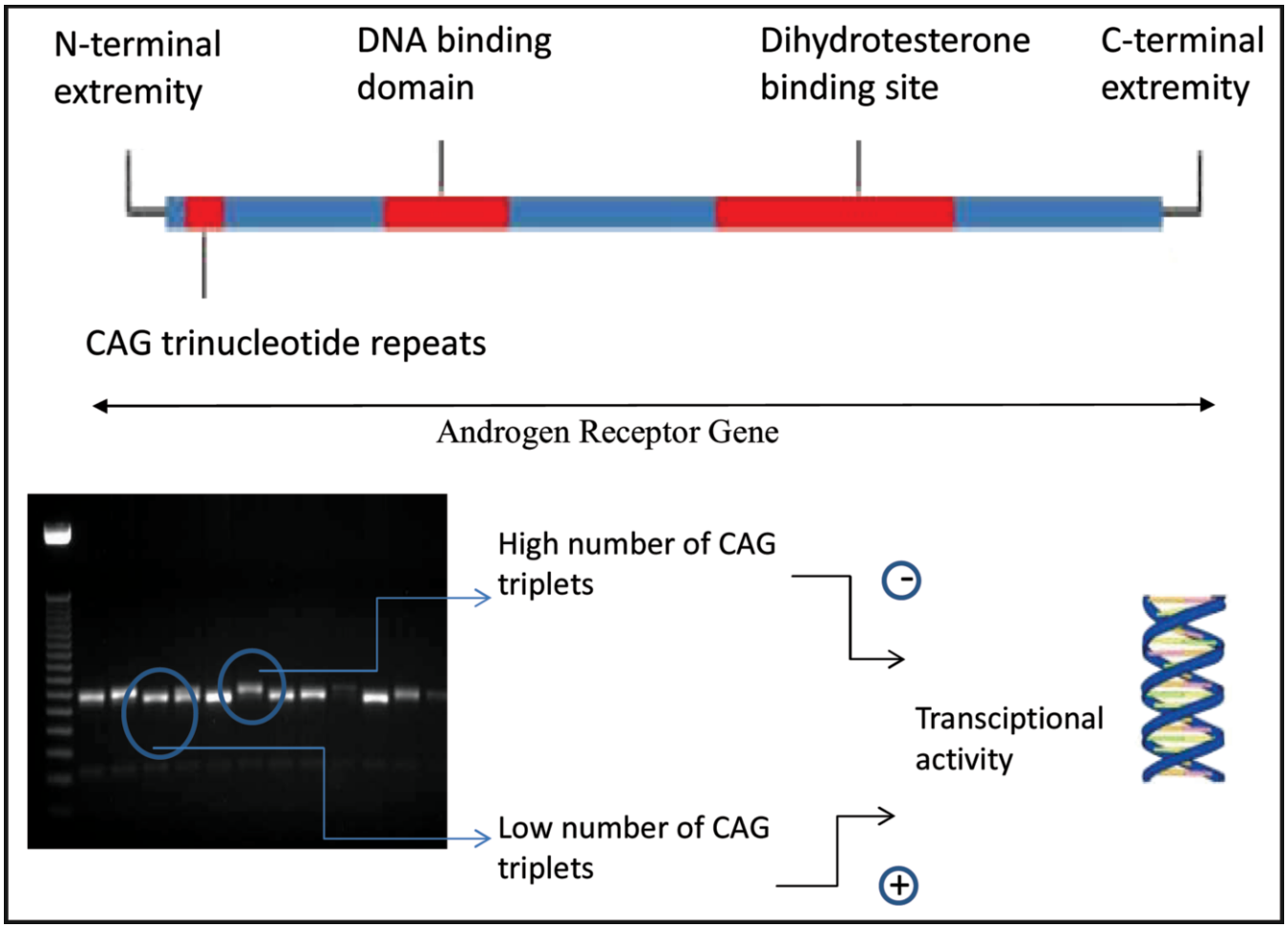


**Figure:** The polymerase chain reaction (PCR) was performed which showed variation in length of CAG fragment on gel electrophoresis in an infertile male subjects.

Androgen Receptor (AR) gene plays an indispensable role in male fertility as it mediates the actions of androgens. The AR gene is located on chromosome Xq11-12 which comprises of 8 exons and 7 introns. Exon 1 encodes a protein associated with transcriptional activity and also

[1,3]Department of Biological & Biomedical Sciences, [2]Aga Khan University, Karachi.
**Correspondence:** Rehana Rehman. Email: drrehana7@gmail.com

has CAG trinucleotide polymorphic repeats.[4] Long (CAG)n repeats in the AR compromise several androgen - dependent functions, especially erectile function. Testosterone is one of the key players in the sexual function by Androgens bind to the androgen receptor which then translocates to the nucleus and hence regulates androgen-responsive gene expression. Mutations in AR gene disrupt function of Androgen receptor, such as missense amino acid substitutions, leading to diminished spermatogenesis and enhanced feminization of individual, resulting in complete androgen insensitivity syndrome.[4]

The AR has a transactivation domain which is susceptible to two forms of polymorphism: a CAG repeat polymorphism which encodes a polyglutamate tract and a GGC repeat which encodes a polyglycine tract. The normal length of AR-CAG trinucleotide repeats range from 18 to 36, though it is typically 22 in Caucasians. The association between AR-CAG trinucleotide repeats and male fertility was established in 1991.[4] Increase in length of the AR-CAG trinucleotide repeats diminish AR function thereby leading to decreased sperm production and spermatogenesis and hence infertility.

A recent study confirmed an association between long trinucleotide repeats of androgen receptor with clinical presentation of premature ejaculatory dysfunction in diabetic patients.[5] Increase in length of AR gene due to increase in AR-CAG trinucleotide repeats is thus a cause of male infertility. The polymerase chain reaction (PCR) was performed which showed variation in length of CAG fragment on gel electrophoresis in infertile male subjects (Figure). After the initial experiment, detection of CAG repeats and comparison of AR gene with fertile males will be performed. Detection of this variance in population of Pakistan can help us to find a cause of male infertility. Variation in CAG in length of AR gene is inversely correlated with gene expression, thus the high number of CAG repeats decrease the transcriptional activity which reduces fertility.

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