

**González Núñez Aidy MD<sup>1</sup>, González del Ángel Ariadna PhD<sup>2</sup>, Martínez Cruz Victor Biol<sup>3</sup>, Alcántara Ortigoza Miguel Ángel PhD<sup>4</sup>, Molecular Biology Department, National Institute of Pediatrics, Mexico City**

## BACKGROUND:

Mexico is globally ranked as one of the countries with the highest incidence of congenital hypothyroidism, with a prevalence rate of 8.1 per 10 000 live births in some regions of the country<sup>1</sup>.

There are few authors that have searched for genetic mutations of *NKX2-1*, a key gene for thyroid development, in patients with isolated congenital hypothyroidism, and they concluded that mutations in this gene can rarely be the origin of congenital hypothyroidism.<sup>2, 3, 4, 5, 6</sup>

A feasible explanation that has been described in others genes is that the etiology of congenital hypothyroidism due to dysgenesis may genetically vary according to the studied population; for this reason we considered important to implement the *NKX2-1* study in Mexico.

## OBJECTIVE:

To search for *NKX2-1* mutations in a sample of mexican patients with confirmatory diagnosis of congenital hypothyroidism (CH) due to thyroid dysgenesis (TD).

## HYPOTHESIS:

*NKX2-1* mutations may cause CH due to TD in mexican population.

## MATERIAL AND METHODS:

This study has an observational, descriptive, transversal and ambispective design. We included 34 mexican newborn patients with CH due to TD.

*NKX2-1* mutations were searched by polymerase chain reaction, single-strand conformation polymorphism (SSCP) and Sanger automated sequencing of the three coding exons.

### Inclusion criteria:

1. Patients with confirmed diagnosis of CH due to TD (by thyroid scintigraphy or ultrasound and measurement of TSH, total T3, total T4, free T3, free T4 and thyroglobulin).
2. Male and female gender.
3. Relatives of patients in whom a mutation has been identified.

## RESULTS:

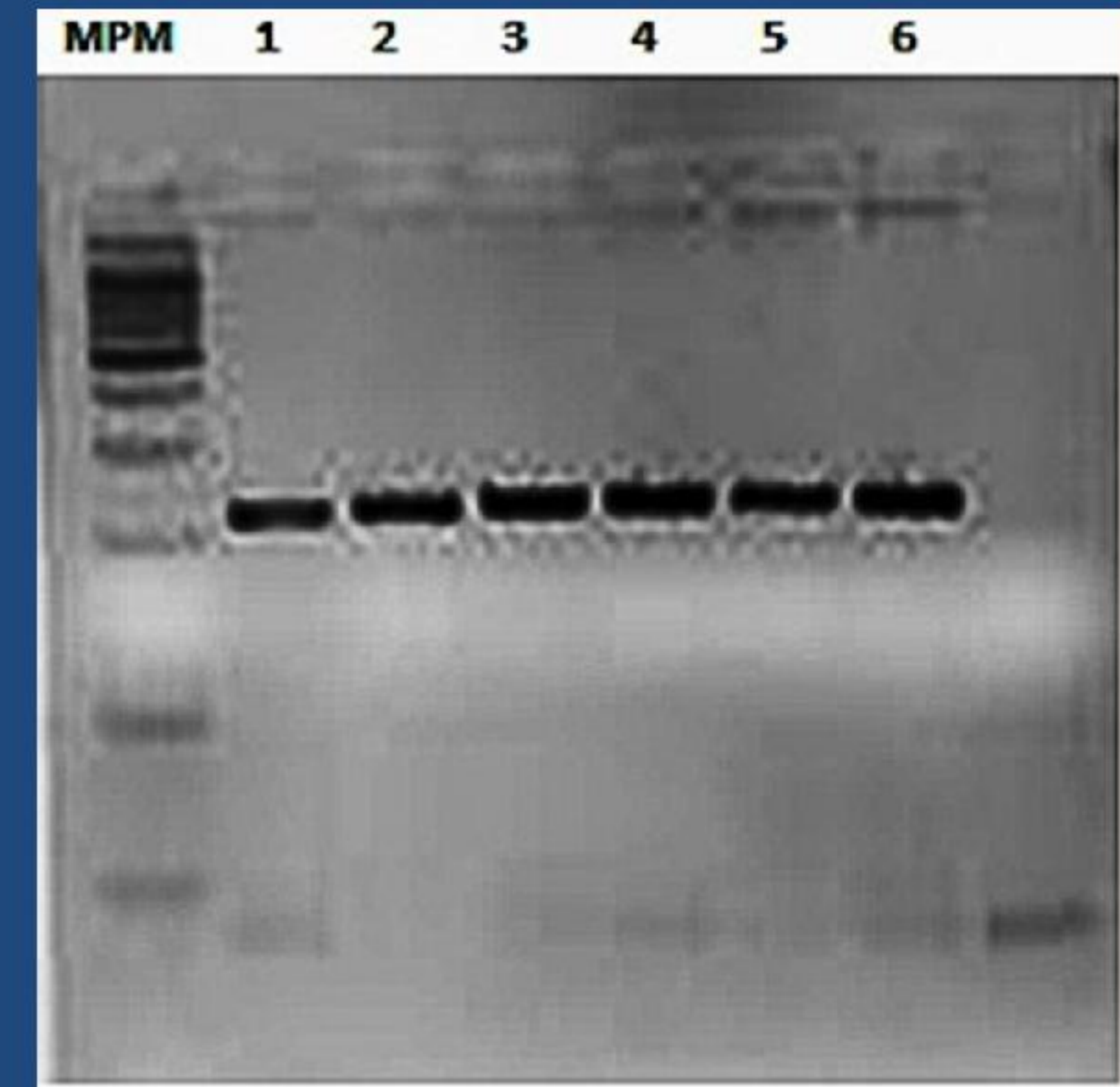
Of the 34 patients included (27 females, 7 males), there was a female gender predominance (3.8:1).

In 97% (n=33) of our patients thyroid scintigraphy was performed. Distribution of TD was found as follows: ectopic thyroid in 57.5% (n=19) and athyreosis in 42.4% (n=14). Thyroid ultrasound was performed in only one patient with athyreosis.

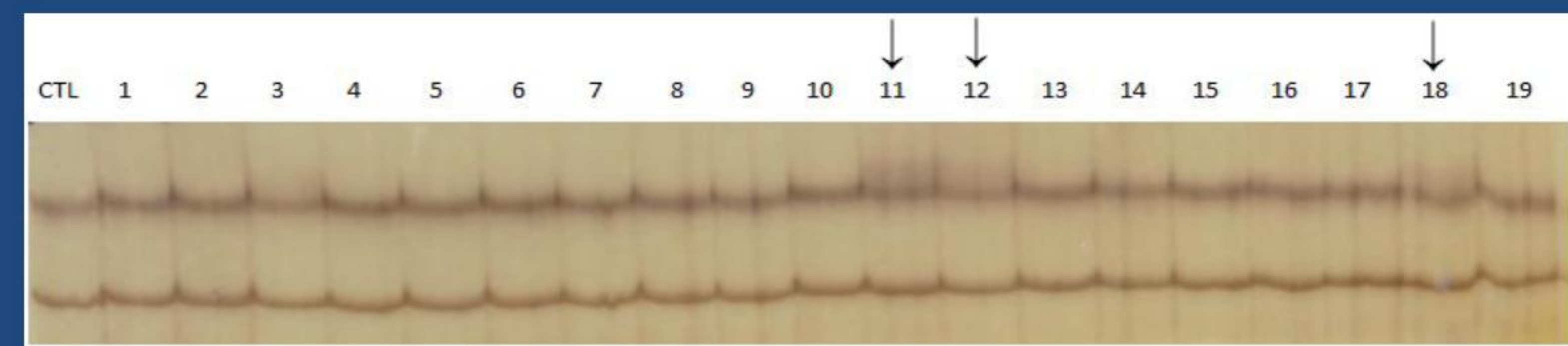
By SSCP, we found an abnormal migration pattern in the first exon of five patients, but we did not find any variation by exon sequencing. The analyzed sequence of *NKX2-1* gene was normal in all of our patients and no other relevant polymorphisms were found.

## REFERENCES:

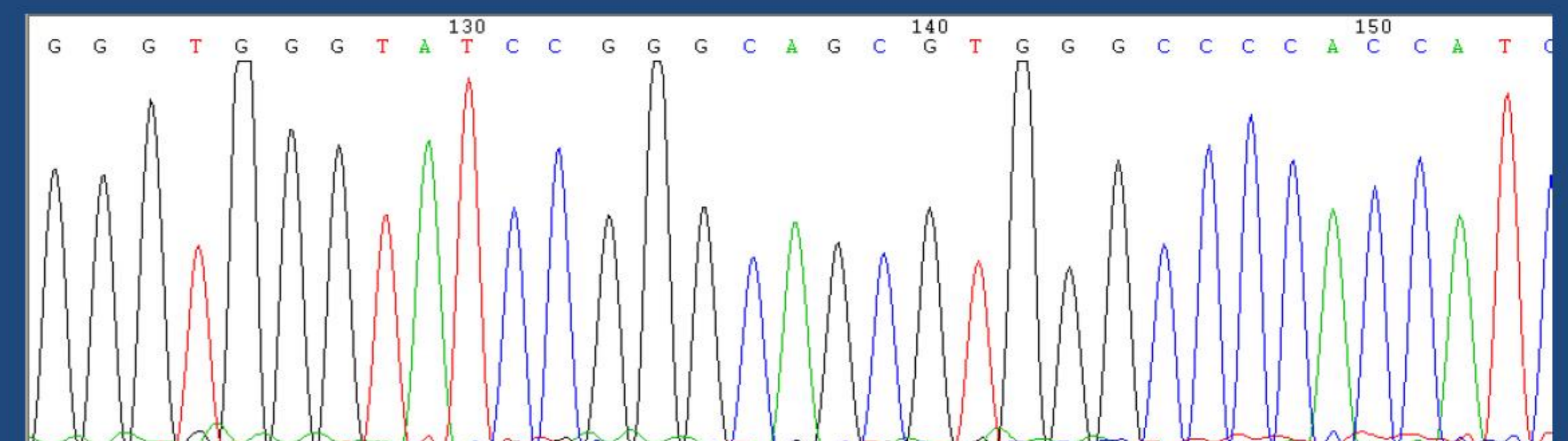
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**Figure 1. Products of PCR on 3% agarose gel (first exon, *NKX2-1* gene) of 6 patients**



**Figure 2. SSCP (first exon, *NKX2-1* gene) that shows a suggestive abnormal migration pattern in three of our five patients (#11, #12 and #18)**



**Figure 3. Partial electropherogram (forward strand, first exon, *NKX2-1* gene) of a patient with a suggestive abnormal migration pattern by SSCP. No pathogenic variants or polymorphisms were identified.**

## CONCLUSION:

In this study the high predominance of CH in mexican population is not explained by mutations or polymorphisms in *NKX2-1* gene, so further studies are needed to analyze other genes involved in thyroid development, such as *NKX2-5* and *FOXE-1* to determine their role as a cause or influencing factor of CH due to TD in our population.