Role of Consanguinity/Familial Incidence in Oral Clefts in Kuwait

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Introduction

Nonsyndromic Cleft lip and palate (NCLP) is one of the most common craniofacial anomalies, with an occurrence of 1.48 in 1000 live births in Kuwait. Environment and genetics play major roles in cleft lip and palate development. Present day evidence supports the idea that inheritability of NCLP is affected by multiple genes.

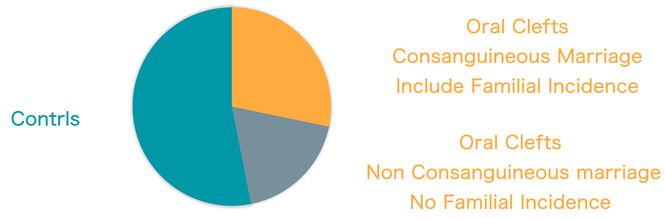
ABCA4 gene provides instructions for making a protein found in the retina, that is active following phototransduction. Studies from brazil and Taiwan confirmed this association with NCLP.

Pax7 is a transcription factor that plays a role in the formation of skeletal muscular tissue, and expressed in the palatal shelf of the maxilla. Similar to ABCA4, the association was identified by GWAS studies and confirmed by other studies conducted in the Polish, Chines, Central European, and Asians. This does not come as a surprise as PAX7 has already been functionally implicated in craniofacial development. Genetic segregation analysis of the families of CLP patients in Kuwait had shown no strong association between consanguinity and the occurrence of facial clefts. However, the specific genetic mutations have never been studied.

Objectives

Investigate the associations of ABCA4 gene variant (rs560426) and PAX7 (rs742071) with occurrence of NCLP in the Kuwaiti population.

Sample Description



Materials and Methods

Blood Collection

- gDNA extraction
- DNA Analysis and Standardization

Genotyping for ABCA4 (rs560426) and PAX7 (rs742071)

- Realtime PCR
- *Taqman* Allelic Discrimination Assay

Association Analysis

- Genotype & Allele Frequency and HWE
- Chi-square Cross tabulation for comparison of genotype distribution between cases and controls
- Logistic Regression Analysis

Results

•Genotype and allele frequencies were in Hardy-Weinberg equilibrium in both groups.

•Chi-Square analysis showed significant association in the frequency distribution between cases and controls in PAX 7 rs742071 (p-value = 0.037)

•Chi-Square analysis showed significant association in the frequency distribution between cases and controls in ABCA4 (rs560426) (p-value = 0.004)

•When segregating patients from consanguineous families from those who are not, no significant associations were found.

Pax 7		Controls	Cases	Total
s742071	GG	31	17	48
	GT	48	39	87
	TT	15	25	40
Totals		94	81	175
		Value	**df**	**Asymptotic Significance (2-sided)**
Pearson Chi Square		6.585[a]	2	.037

HWE for controls p-value =0.615

ABCA4		Controls	Cases	Total
rs560426	GG	8	17	25
	GA	49	22	71
	AA	38	33	71
Totals		95	72	167
		Value	**df**	**Asymptotic Significance (2-sided)**
Pearson Chi Square		10.899a	2	.004

HWE for controls p-value =0.155

Discussion and Conclusion

The limited power of the samples cannot be excluded as a reason for the lack of association when segregating consanguineous families. Our findings however, confirmed the importance of 1p36 (rs742071), and 1p22.1 (rs560426) loci in the NCLP susceptibility in the Kuwaiti population.

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