

## Introduction

Non-syndromic cleft lip and palate (NCLP) is one of the most common craniofacial anomalies with the occurrence of 1.48/1000 live births in Kuwait. Reproducibility and population-based studies have suggested the association of the Bone Morphogenetic Protein 4 (BMP4 rs17563) with the increased development of NCLP. The protein product of this gene is important in the regulation of gene expression needed for bone and cartilage development. Some studies have also reported a potential role of BMP4 expression in the signal pathways for lip and palate fusion.

## Objectives

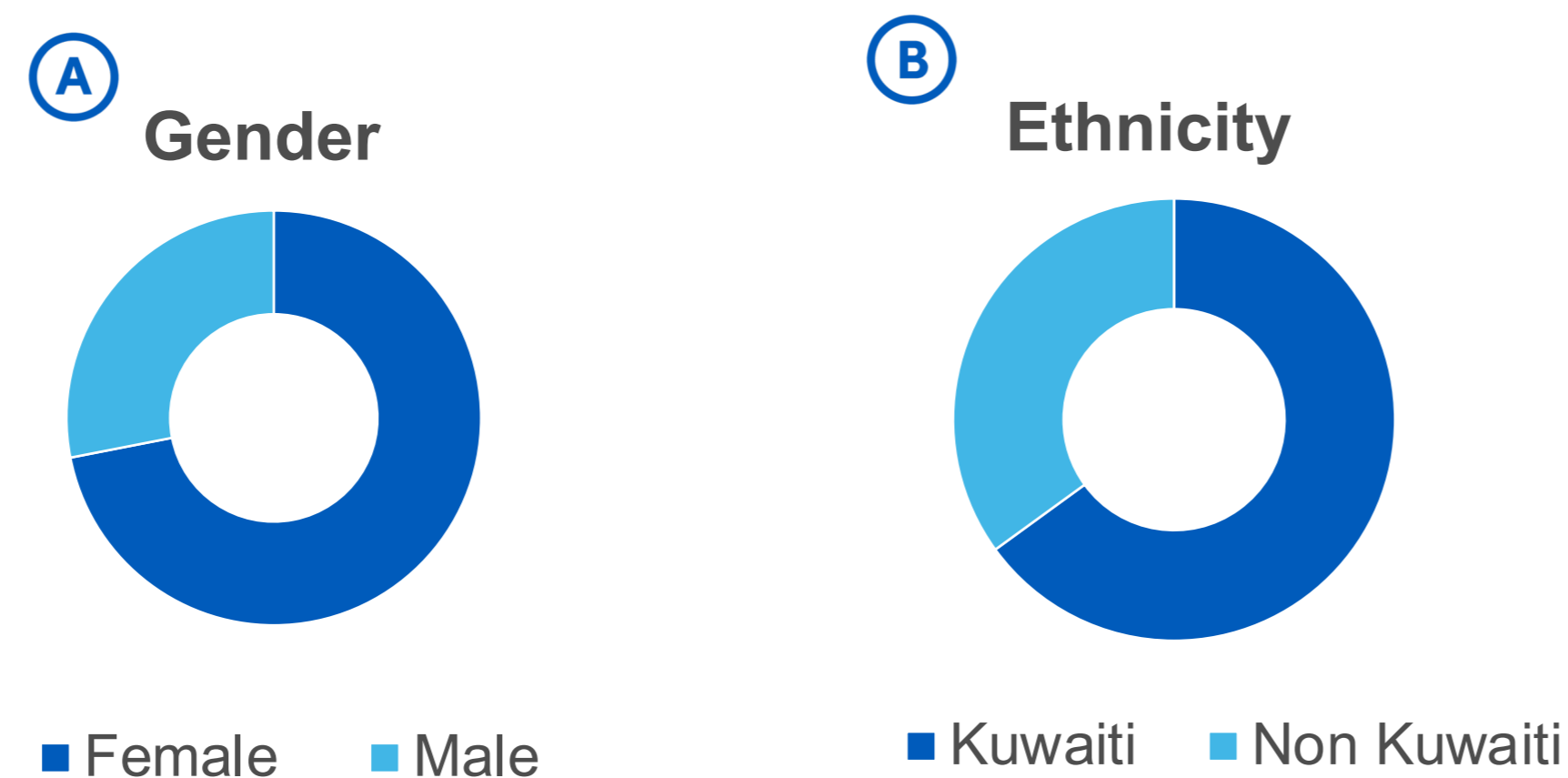
Investigate the association of a common human bone morphogenetic protein 4 (BMP4) gene variant (rs17563) with occurrence of NCLP in the Kuwaiti population.

## Sample Description

A total 212 samples were included:

- 120 Cases of confirmed NCLP (A, B)
- 95 random controls

## Demographic Profile



## Methods

### Blood Collection

- gDNA extraction
- DNA Analysis and Standardization

### Genotyping for BMP4 rs17563

- Realtime PCR
- Taqman Allelic Discrimination Assay

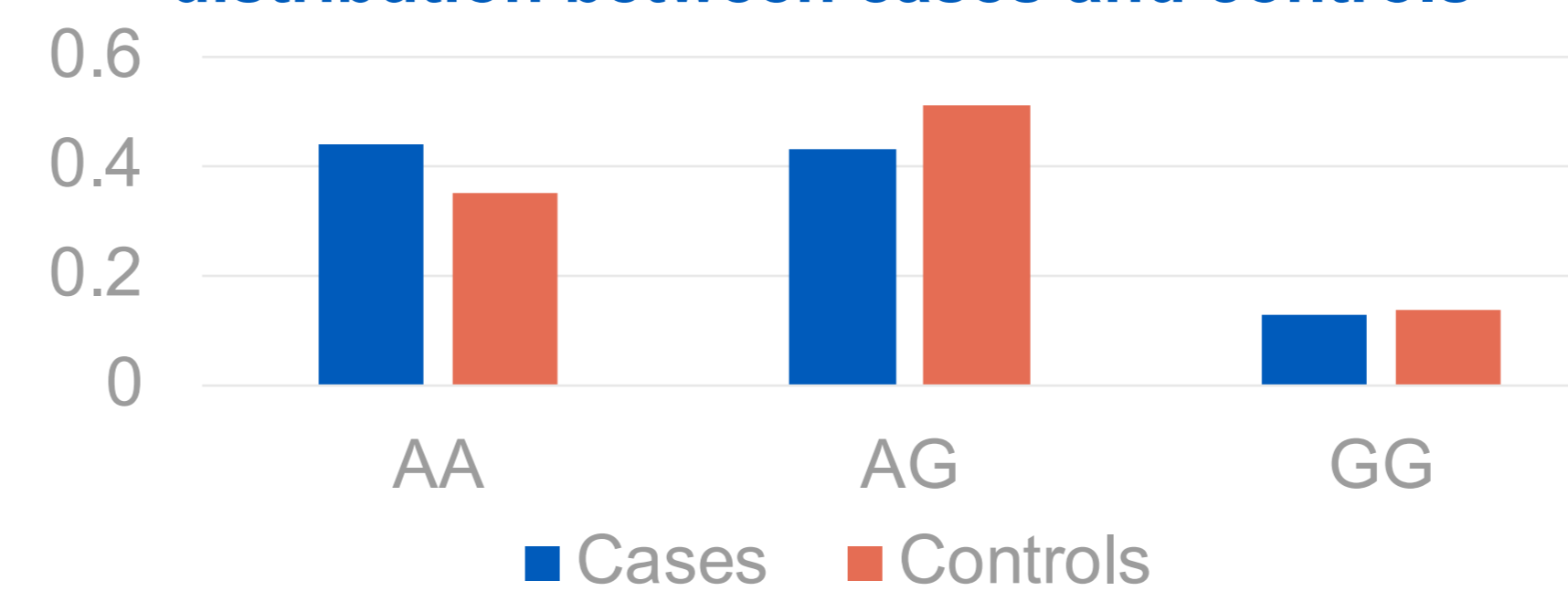
### Association Analysis

- 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 using cross-tabulations did not show any significant difference in the frequency distribution between cases and controls.
- Logistic regression analysis after adjusting for gender and ethnicity was done to estimate the odds ratios (ORs) with the corresponding 95% confidence intervals (CIs) to test for the association of BMP4 rs17563 with NCLP did not reveal a significant association

### BMP4 rs17563 Genotype and allele frequency distribution between cases and controls



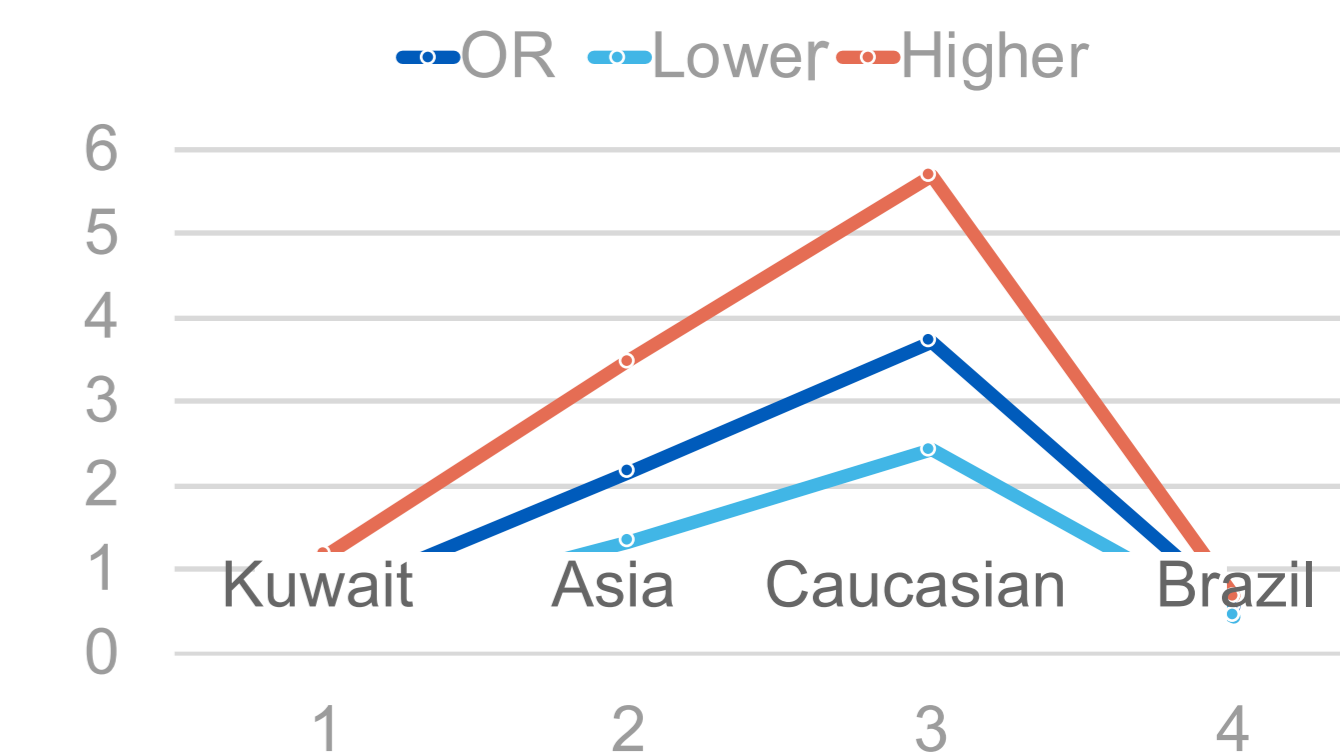
### Logistic Regression after adjusting for gender and ethnicity

	OR	P-value	CI Lower	CI Upper
rs17563	0.778	0.223	0.519	1.165
Gender	1.032	0.913	0.592	1.797
Ethnicity	1.697	0.062	0.973	2.959

## Discussion and Conclusion

- The OR for the Asian and Caucasian populations indicate an increased risk to develop NCLP. However, the analysis indicates a “protective” role for the Kuwaitis and Brazilians. The OR for the Kuwaiti population is not significant due to the wide range of 95% CI.
- The inconsistency of the results among different populations might indicate that the association is ethnic specific.
- It is strongly recommended that sample size is increased and to further investigate the genetic association of other variants.

### Logistic Regression Analysis in Different Ethnicities



	OR	CI: 95% Interval	
		Lower	Higher
Kuwait	0.67	0.382	1.174
Asia	2.16	1.34	3.47
Caucasian	3.71	2.43	5.69
Brazilian	0.56	0.45	0.69



For More Information and References



## ACKNOWLEDGMENT

This research is funded by the Kuwait Foundation for the Advancement of Sciences Grant

#PR17-13DS-01

The Use of General Facility GS01/02; Biotechnology Center, Faculty of Science, Kuwait University