

Birth prevalence of non-syndromic orofacial clefts in Saudi Arabia and the effects of parental consanguinity

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ABSTRACT

الأهداف: لوصف الخصائص وانتشار الشق الفموي الوجهي غير المرتبط بمتلازمة في الرياض في 3 مدن رئيسية في المملكة، وقمنا بتقييم آثار قرابة الأبوين على هذه الظاهرة.

الطريقة: جميع الرضع (114,035) الذين ولدوا في 3 مراكز في الرياض و 6 مشافي في جدة و المدينة خلال الفترة ما بين يناير 2010م إلى ديسمبر 2011م تم فحصهم. وقد تم تحديد الحالات المصابة بالشق الفموي الوجهي غير المرتبط بمتلازمة (113) حالة من خلال توثيق الفحص السريري و مقابلة الأبوين. لقد تم تأكيد تشخيص حالات الشق الفموي الوجهي غير المرتبط بمتلازمة بالرجوع إلى السجلات والتواصل مع أطباء الأطفال وحديثي الولادة. لقد تم اختيار (233) حالة للجنسين لحالات الشق الفموي غير المرتبط بمتلازمة وولدوا بنفس المستشفيات بنفس الفترة وذلك لمواصلة تحليل آثار زواج الأقارب على الشق الفموي غير المرتبط بمتلازمة.

النتائج: كانت نسبة انتشار الحالات 1.17/1000 مولود في الرياض، و 1.17/1000 مولود في العموم. وكانت الشفة المشقوقة 0.47/1000 مولود، والشفة المشقوقة مع شق سقف الحنك 0.42/1000 مولود، وشق سقف الحنك 0.28/1000 مولود. كان ارتباط شق سقف الحنك بشكل كبير مع زواج الأقارب، $p=0.047$ ، $OR: 2.5$ & $95\% CI: 1$ حتى 6.46 ،

الخلاصة: انتشار الشق الفموي غير المرتبط بمتلازمة في الرياض لوحدها وفي 3 مدن رئيسية في المملكة العربية السعودية كان أقل انتشار في العالم. يعني. بينما كان انتشار الولادة CLP مقارنة للأرقام العالمية، وCL: بلغت نسبة CLP العالية، و فقط CP كان مرتبطا بشكل كبير مع زواج

Objectives: To describe the characteristics and prevalence of non-syndromic orofacial clefting (NSOFC) and assess the effects of parental consanguinity on NSOFC phenotypes in the 3 main cities of Saudi Arabia.

Methods: All infants (114,035) born at 3 referral centers in Riyadh, and 6 hospitals in Jeddah and Madinah between January 2010 and December 2011 were screened. The NSOFC cases (n=133) were identified and

data was collected through clinical examination and records, and information on consanguinity through parent interviews. The diagnosis was confirmed by reviewing medical records and contacting the infants' pediatricians. Control infants (n=233) matched for gender and born in the same hospitals during the same period, were selected.

Results: The prevalence of NSOFC was 1.07/1000 births in Riyadh, and 1.17/1000 births overall; cleft lip (CL) was 0.47/1000 births, cleft lip and palate (CLP) was 0.42/1000 births, and cleft palate (CP) was 0.28/1000 births. Cleft palate was significantly associated with consanguinity ($p=0.047$, odds ratio: 2.5, 95% confidence interval: 1 to 6.46), particularly for first cousin marriages.

Conclusion: The birth prevalence of NSOFC in Riyadh alone, and in the 3 main cities of Saudi Arabia were marginally lower than the mean global prevalence. While birth prevalence for CLP was comparable to global figures, the CL:CLP ratio was high, and only CP was significantly associated with consanguinity.

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Non-syndromic orofacial clefting (NSOFC), including isolated cleft lip (CL), cleft lip and palate (CLP), and isolated cleft palate (CP), is the most common craniofacial defect worldwide with an estimated mean global prevalence of 1.25/1000 live births.¹ However, the prevalence of NSOFC varies geographically and across different ethnic groups.² Although the ethnicity of the Middle East is considered Caucasian,^{3,4} geographically it is located between 3 continents (Asia, Africa, and Europe), which makes it unique and, in reality, a mixture of 3 ethnicities. A small number of studies have measured the prevalence of NSOFC in Saudi Arabia and neighboring countries with the reported prevalence ranging from 0.3 to 2.19/1000 births,⁵⁻⁹ and a mean value for all studies of 1.25/1000 births.¹⁰ In addition, consanguineous relationships have been suggested to increase the prevalence of congenital anomalies.¹¹ These were also reported to be associated with NSOFC in a meta-analysis carried out on 16 studies that assessed the relationship between NSOFC and paternal consanguinity.¹² Saudi Arabia, one of the largest countries in the Middle East, has a high rate of consanguineous marriage that varies between regions.¹³ Riyadh, which is the capital city of Saudi Arabia with a population of approximately 7.5 million and birth prevalence of 38,000/year,^{14,15} has a consanguinity marriages prevalence of 60%.¹⁶ The aims of this study were to 1) describe the characteristics and prevalence of NSOFC (CL, CLP, and CP) in Riyadh (the capital city in the central region of Saudi Arabia), 2) describe the prevalence of NSOFC phenotypes, and 3) the relationship between these and consanguinity in Saudi Arabia.

Methods. This study was conducted at 3 medical referral hospitals in Riyadh: King Fahad Medical City (1000 beds), King Saud Medical City (1200 beds), and Riyadh National Guard Hospital (690 beds). Riyadh constitutes approximately 25% of the Saudi population, which is almost 30,000,000.¹⁴ Data from 2

previously published studies, conducted in Jeddah and Madinah, were also included.^{17,18} Jeddah and Madinah are 2 major cities in the Western Region of Saudi Arabia that constitute approximately 35% of the Saudi population.¹⁴

The inclusion criteria for Riyadh matched those of the Jeddah and Madinah studies: all infants born at the study hospitals between January 2010 and December 2011 were included. The prevalence was calculated as the proportion of infants with NSOFC out of the total number of births, excluding cases of syndromic orofacial clefting.

The sample size was calculated using Open Source Epidemiologic Statistics for Public Health (OpenEpi) online software (<http://www.openepi.com/oe2.3/menu/openepimenu.htm>). Factors used in the calculation were the estimated population size (98,000 births/year¹⁵) and the predicted prevalence based on the mean global prevalence figures (1.25/1000 births) and 95% confidence intervals (CI). This provide a sample size of 61,055 infants to measure the prevalence of NSOFC in Saudi Arabia. We screened 40,005 infants from 3 hospitals in Riyadh and, by adding data from the Jeddah and Madinah studies, collected data on a total of 114,035 infants. A case-control study design was used to assess the relationship between parental consanguinity and NSOFC. The study group included infants born with NSOFC (n=133) in Riyadh, Jeddah, and Madinah and the control group included 233 unaffected infants matched for gender and location.

This study was approved by the King Abdulaziz University Research Committee, the Institutional Research Review Board (IRB) of the Ministry of Health, and the Military Hospital. Consent to participate was given by parents.

Procedure. Infants born with NSOFC were identified, and the information was passed to a research coordinator. To ensure optimal enrolment, eligible patients were actively pursued every 2 weeks through nursing staff working at the neonatal units or neonatal intensive care units of the respective hospitals. Data was collected through clinical examinations and parental interviews. In addition, a NSOFC diagnosis was confirmed by reviewing medical records and contacting the infants' pediatricians. The total number of infants born with NSOFC in these hospitals over the study period was retrieved from the statistical records of each of the hospitals for that period. The NSOFC prevalence was measured by comparing the number of NSOFC cases to the total number of births at each hospital. The NSOFC phenotypes were classified according to LAHSHAL classification,¹⁹ which subdivides CL

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according to side (right, left, or bilateral) and complete/incomplete (with/without Simonart's band). These subdivisions were used to classify the extent or severity of clefting of the lip in cases of CL and CL with or without cleft palate (CL[P]).¹

A questionnaire interview with mothers was conducted to obtain data on parental consanguinity, and type of consanguinity (first cousins, first cousins once removed, second cousins, and other type of relatives). The matched control group was used to measure the effects of consanguinity on NSOFC phenotypes and severity.

Statistical analysis. Data were analyzed using the Statistical Package for Social Sciences version 16.0 (SPSS Inc., Chicago, IL, USA). Descriptive statistics, such as frequency and percentage, on the epidemiology of NSOFC were analyzed. The Chi square test was used to test for association between consanguinity and the type of NSOFC and severity of CL(P). The significance level was set at $p < 0.05$. The odds ratio (OR) and 95% confidence interval (CI) was used to measure the effect of consanguinity on NSOFC risk.

Results. Prevalence of NSOFC in Riyadh. At the 3 hospitals in Riyadh, 43 infants were born with NSOFC between January 2010 and December 2011 out of 40,005 births, giving a birth prevalence of 1.07/1000 births. The prevalence of CL was 0.32/1000 births, of CLP 0.35/1000 births, and of CP 0.4/1000 births (Table 1). Left incomplete CL was the most common NSOFC sub-phenotype, seen in 6 (22.2%) infants (Table 2). Associated anomalies were diagnosed in 10 cases (23.3%) of cases.

Overall prevalence of NSOFC in Saudi Arabia.

When the data from Jeddah and Madinah,^{14,15} were added to that from Riyadh, to give a total of 133 births during the study period, a prevalence of 1.17/1000 births was obtained. The prevalence of CL was 0.47/1000 births, of CLP 0.42/1000 births, and of CP 0.28/1000 births. The prevalence of NSOFC was higher in Madinah (1.88/1000 births) than in Jeddah (0.81/1000 births), and Riyadh (1.07/1000 births) (Table 1). Table 2 shows the distribution of NSOFC sub-phenotype according to gender in all 3 cities. Of the 70 cases of unilateral CL(P), the prevalence of left sided CL(P) (CL 28 cases, 21.1%, and CLP 16 cases, 12%) was higher than that of right-sided CL(P) (CL 13 cases, 9.8%, and CLP 13 cases, 9.8%). The frequency of bilateral CLP (19 cases, 14.3%) was higher than that of bilateral CL (12 cases, 9%). Out of the 101 CL(P) cases, the frequency of incomplete clefting of the lip (58 [57.4%]) was higher than complete clefting of the lip (43 [42.6%]). The prevalence of CL(P) was higher in males (66 cases, 65.3%) than females (35 cases, 34.6%). On the other hand, the same number of males and females with CP was encountered (16 cases). In addition, there was a statistically significant difference in the distribution of the 3 NSOFC phenotypes (CL, CLP, and CP) according to gender ($p = 0.035$). After Chi square adjustment using Bonferroni correction, CL was significantly higher in males than in females ($p < 0.05$).

Effects of city of birth and consanguinity on NSOFC phenotype severity. The prevalence of parental consanguinity was measured for all infants born with NSOFC. Parental consanguinity information was missing in 10 cases, and these were excluded from the analysis. The prevalence of consanguinity among infants

Table 1 - Birth prevalence of non-syndromic orofacial clefting (NSOFC) by place of birth and phenotype in Saudi Arabia between January 2010 and December 2011.

City	Total births	CL	CLP	CP	Total NSOFC	NSOFC prevalence/1000 births
<i>Riyadh</i>						
King Saud Medical City	13,252	6	4	6	16	1.2
Riyadh National Guard Hospital	16,926	2	6	9	17	1
King Fahad Medical City	9,827	5	4	1	10	1
Total	40,005	13	14	16	43	
Prevalence/1000 births	1,000	0.32	0.35	0.4		1.07
<i>Jeddah</i>						
	45,896	16	15	6	37	
Prevalence/1000 births	1,000	0.35	0.33	0.13		0.81
Madinah	28134	24	19	10	53	
Prevalence/1000 births	1,000	0.85	0.67	0.36		1.88
Overall births	114,035	53	48	32	133	
Overall prevalence/1000 births	1,000	0.47	0.42	0.28		1.17

CL - cleft lip, CLP - cleft lip and palate, CP - cleft palate

with NSOFC in Saudi Arabia was 65.9% (81 cases): 56.1% in Riyadh (23 cases), 77.4% in Madinah (41 cases), and 58.6% in Jeddah (17 cases). There was no relationship between gender and parental consanguinity (χ^2 : 0.45, and $p=0.502$). The prevalence of consanguinity was higher for CP (78.6%) than for CL(P) (61.1%); however, the difference was not statistically significant (χ^2 : 2.61 and $p=0.106$). In addition, the prevalence of severe CL(P) (complete clefting of the lip or a bilateral cleft) was higher in infants with consanguineous parents

than that in infants with non-consanguineous parents; however, these differences were not significant (χ^2 : 2.38 and $p=0.123$; and χ^2 : 0.39 and $p=0.534$, respectively) (Table 3). Consanguinity was more prevalent in infants with NSOFC, including all its phenotypes, compared with controls (Table 4). However, the relationship was only statistically significant for CP ($p=0.047$, OR: 2.5, and 95% CI: 1 to 6.46). The highest prevalence for CP was for first cousin consanguinity, at 72.8% compared with 58.9% for controls.

Table 2 - Distribution of NSOFC sub-phenotypes in Saudi Arabia by place of birth and gender.

Phenotype	Sub-phenotype	Riyadh, Saudi Arabia			Overall, Saudi Arabia		
		Male	Female	Total	Male	Female	Total
<i>Cleft lip</i> N=53 Male: 40 Female: 13	Right incomplete	1 (3.7)	1 (6.3)	2 (4.7)	7 (8.5)	2 (3.9)	9 (6.8)
	Right complete	0 (22.2)	1 (6.3)	1 (2.3)	2 (2.4)	2 (3.9)	4 (3.0)
	Left incomplete	6	1 (6.3)	7 (16.3)	13 (15.9)	5 (9.8)	18 (13.5)
	Left complete	1 (3.7)	1 (6.3)	2 (4.7)	9 (11.0)	1 (1.9)	10 (7.5)
	Bilateral incomplete	1 (3.7)	0	1 (2.3)	8 (9.8)	2 (3.9)	10 (7.5)
	Bilateral complete	0	0	0	1 (1.2)	1 (1.9)	2 (1.5)
<i>Cleft lip and palate</i> N=48 Male: 26 Female: 22	Right incomplete	0	0	0	5 (6.1)	6 (11.8)	11 (8.3)
	Right complete	1 (3.7)	1 (6.3)	2 (4.7)	2 (2.4)	0	2 (1.5)
	Left incomplete	1 (3.7)	1 (6.3)	2 (4.7)	2 (2.4)	2 (3.9)	4 (3.0)
	Left complete	1 (3.7)	3 (18.8)	4 (9.3)	3 (3.7)	9 (17.6)	12 (9.0)
	Bilateral incomplete	1 (3.7)	0	1 (2.3)	4 (4.9)	2 (3.9)	6 (4.5)
	Bilateral complete	4 (14.8)	1 (6.3)	5 (11.6)	10 (12.2)	3 (5.9)	13 (9.8)
<i>Cleft palate (n=32)</i> Male: 16 Female: 16	Cleft lip	10 (37)	6 (37.5)	16 (37.2)	16 (20.0)	16 (31.4)	32 (24.1)
	Total	27 (100)	16 (100)	43 (100)	82 (100)	51 (100)	133 (100)

Data are expressed as number and percentage (%). NSOFC - non-syndromic orofacial clefting, CL - cleft lip, CLP - cleft lip and palate, CP - cleft palate

Table 3 - Consanguinity and NSOFC phenotype, gender, and severity in Saudi Arabia.

Variables	Consanguinity n (%)	Non- consanguinity n (%)	Total n (%)	x ² (P-value)
<i>Gender</i>				
Male	49 (63.6)	28 (36.4)	77 (100)	0.45 (0.502)
Female	32 (69.6)	14 (30.4)	46 (100)	
Total	81 (65.9)	42 (34.1)	123 (100)*	
<i>Type of NSOFC</i>				
CL(P)	59 (62.1)	36 (37.9)	95 (100)	2.61 (0.106)
CP	22 (78.6)	6 (21.4)	28 (100)	
Total	81 (65.9)	42 (34.1)	123 (100)*	
<i>CL in CL(P)</i>				
Complete	33 (70.2)	14 (29.8)	47 (100)	2.38 (0.123)
Incomplete	24 (54.5)	20 (45.5)	44 (100)	
Total	57 (62.6)	34 (34.4)	91 (100)	
<i>CL site in CL(P)</i>				
Bilateral	20 (66.7)	10 (33.3)	30 (100)	0.39 (0.534)
Unilateral	39 (60.0)	26 (40.0)	65 (100)	
Total	59 (62.1)	36 (37.9)	95 (100)	
NSOFC - non-syndromic orofacial clefting, CL - cleft lip, CL(P) - cleft lip with/without cleft palate. *The total number is less than 133 due to 10 cases of missing information				

NSOFC - non-syndromic orofacial clefting, CL - cleft lip, CL(P) - cleft lip with/without cleft palate. *The total number is less than 133 due to 10 cases of missing information

Table 4 - Comparison of NSOFC and controls for frequency and type of consanguineous marriage in Saudi Arabia.

Consanguineous	NSOFC	CL	CLP	CP)	Control
<i>Consanguinity</i>					
Yes	81 (65.9)	31 (63.3)	28 (60.9)	22 (78.6)	138 (59.2)
No	42 (34.1)	18 (36.7)	18 (39.1)	6 (21.4)	95 (40.8)
Total	123 (100)	49 (100)	46 (100)	28 (100)	233 (100)
<i>P</i> value	0.222	0.6	0.836	0.047†	
OR 95% (CI)				2.5 (1-6.46)	
<i>Type of consanguinity</i>					
1 st cousins	44 (56.4)	16 (53.3)	12 (46.2)	16 (72.8)	76 (58.9)
1 st cousins once removed	4 (5.1)	3 (10.0)	1 (3.8)	0	8 (6.2)
2 nd cousins	14 (18.0)	6 (20.0)	5 (19.2)	3 (13.6)	18 (14.0)
Other relatives	16 (20.5)	5 (16.7)	8 (30.8)	3 (13.6)	27 (20.9)
Total	78* (100)	30* (100)	26* (100)	22 (100)	129 (100)

Data are expressed as number and percentage (%), NSOFC - non-syndromic orofacial clefting, CL - cleft lip, CLP - cleft lip and palate, CP - cleft palate, OR - odds ratio, 95% CI - 95% confidence intervals. *The total number is lower than the full dataset due to missing information †Significant relationship

Discussion. This study describes the characteristics and prevalence of NSOFC in Riyadh, and overall for the cities of Riyadh, Jeddah, and Madinah, in Saudi Arabia. We have also assessed the impact of consanguinity on the pattern and severity of NSOFC in Saudi Arabia. Although the data for Jeddah and Madinah were published previously, this paper combines these data with our dataset for a third major city, Riyadh, allowing a more comprehensive picture of oral cleft prevalence in Saudi Arabia.

The prevalence of NSOFC for Riyadh over the 2-year period of the study was 1.07/1000 live births, which is higher than the 0.3/1000 births previously reported for Riyadh.⁸ However, our study had a more comprehensive methodology for ascertainment. Moreover, the prevalence of NSOFC in Riyadh (1.07/1000 live births) and overall (1.17/1000 live births) was marginally lower than the mean global prevalence (1.25/1000 live births).¹ It is also lower than the prevalence reported by Sabbagh et al¹⁰ for Saudi Arabia and its neighboring countries (1.25/1000 live birth). However, Iran, which is another large Middle East country, showed a lower prevalence of NSOFC (1/1000 births).²⁰

Jeddah showed the lowest prevalence of all cities, while Madinah showed the highest; the prevalence for Madinah was also higher than the mean global prevalence. This suggests a genetic and geographical influence on the prevalence of NSOFC between regions of Saudi Arabia related to the fact that NSOFC is a multifactorial birth defect.²¹ The prevalence of CL is higher than that of CLP, particularly in Madinah, differing from global findings, with previous studies reporting a higher prevalence of CLP than of CL.²²

The higher consanguinity in Madinah compared with Jeddah¹⁶ suggests that consanguinity might have played a role in NSOFC phenotype and, thus, the higher prevalence of CL. Furthermore, studies in countries with low consanguinity show a higher prevalence of CLP than that of CL.^{23,24} The higher prevalence of CL(P) in males is similar to global findings.¹ However, CP prevalence (similar prevalence for both gender) was not parallel to the global figures, which report a higher prevalence of CP in females compared with males. A local etiological factor or poor ascertainment of CP could lie behind the increase in CP ratio in males during the 2-year period that was included in this research. Additional studies are needed to further clarify the relationship between various risk factors and the manifestation of CP, and how this might differ between genders.

In children with unilateral CL(P) left-sided clefts were more common than right. This is similar to other studies,^{9,25,26} although there is no clear explanation as to why the left side of the lip is more prone to clefting.¹ The possibility has been raised that the right side may have better hemodynamic perfusion as fetal head vessels on the right side leave the aortic arch closer to the heart.²⁷ The prevalence of bilateral CL (9%) was similar, but bilateral CLP (14.3%) was lower than the prevalence in previous studies, which showed approximately 10% for CL and 30% for CLP.²⁸⁻³⁰

Understanding the pattern of NSOFC sub-phenotypes could inform future genetic research and establish a more personalized approach towards controlling NSOFC in the future. However, the problem in contemporary research is the failure to sub-phenotype into CL and CLP in the light of emerging

evidence of genetic distinction between these;³¹ and it is logical to assume that complete and incomplete clefts have different origins,³² and therefore there may be a difference in aetiology (genetic and environmental). A disadvantage is that larger numbers overall are needed for statistical handling.

The prevalence of associated anomalies in Riyadh reported in this study was 23.3%, which is higher than those reported in previous reports in Middle East countries ranging from 13-18%,¹⁰ and Jeddah (17.7%).¹⁸ However, other studies have reported values as high as 63%.^{6,33,34} This could be related to methodological differences such as variable diagnoses of associated anomalies and incomplete ascertainment. In addition, it was reported that 7.1% of NSOFC cases diagnosed as isolated cleft at birth, were found to be associated with other birth anomalies, after one year.³⁵ Parental consanguinity and its relationship to oral clefting was assessed in a systematic review carried out on all case-control papers that reported the effect of parental consanguinity on NSOFC. Although the systematic review suggested a positive relationship,¹² it reported a high level of heterogeneity among the included studies. Saudi Arabia has a high rate of consanguineous marriage that varies between regions.¹³ The prevalence of consanguinity in NSOFC in this study was 65.9%, higher than the prevalence of 54.4% reported by Al-Johar et al³⁶ for a hospital-based cross sectional study of craniofacial cases in King Faisal Specialized Hospital and Research Centre in Riyadh. It is also higher than the prevalence reported by El Mouzan et al,¹⁶ and El-Hazmi et al¹³ for the general Saudi population (57% and 57.7%). The prevalence of consanguinity for NSOFC infants in each city in our study was: Madinah (77.4%), Riyadh (56.1%), and Jeddah (58.6%); and in El Mouzan et al¹⁶ were: 67.2%, 60%, and 44%. Of all NSOFC infants with consanguineous parents, 44 couples (54.3%) were first cousins, slightly higher than El-Hazmi et al³⁴ who reported consanguinity of 41% in the general population.

The higher prevalence of consanguineous marriages in NSOFC compared with the general population could indicate that it is a risk factor in the etiology of NSOFC; this is supported by previous research.^{34,37} However, to confirm this relationship, we used a case-control study design. The prevalence of parental consanguinity was higher for NSOFC and its sub-phenotypes compared with controls; however, the relationship was only statistically significant for CP, with a doubling of the risk. Sabbagh et al¹² in their systematic review reported a higher OR for CP (OR: 1.89 and 95% CI: 1.14 - 3.13) compared with CL(P)

(OR: 1.56 and 95% CI: 1.18 - 2.07 for CL(P)). In addition, in the Alamoudi et al¹⁸ study conducted in Jeddah, a significant relationship was reported between consanguinity and CP ($p=0.039$). This could explain why the birth prevalence of CP in Riyadh and Madinah was higher than in Jeddah, which appears to have the lowest consanguinity in this and other reported studies. Moreover, the higher prevalence of consanguinity in severe CL(P) cases could indicate that parental consanguinity could influence the pattern and severity of NSOFC. When assessing the type of consanguinity, a higher percentage of first cousin consanguineous marriages (72.7%) were seen in families with CP compared with controls (58.9%) and compared to CL(P) (approximately 50%).

Future research on the prevalence of cleft palate sub-phenotypes and its etiology in each region in Saudi Arabia is warranted. Additionally, stillbirths were not included in this study, which might have caused some bias.^{5,38} However, the impact of stillbirth on prevalence is expected to be low as it accounts for 13.2/1000 births recorded by the Ministry of Health, Saudi Arabia.¹⁵ Larger scale national research that includes the private sector, which provides healthcare to approximately 20% of the Saudi population,³⁹ should be considered to describe NSOFC prevalence in the future. Studies that define the relationship between each NSOFC sub-phenotype and, different environmental and genetic risk factors are recommended.

This study contributes to the World Health Assembly recommendation in 2010 that all member of the states should pay attention to birth defects (including OFC) as a significant contributor to the global burden of disease, both in terms of mortality and morbidity. It measured the prevalence of NSOFC phenotype among Saudis' infants in the western and central region giving a prevalence marginally lower than the mean global prevalence. While birth prevalence for CLP was comparable to global figures, the CL:CLP ratio was high. It also assessed the relationship between consanguinity and both CL(P) and CP reporting that CP was the only NSOFC phenotype that showed a significant relationship with paternal consanguinity.

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 - The following are the typical headings:

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Methods (setting, date of study, design, subjects, intervention and analysis)

Results (findings, data and statistical tests) and

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