

Risk factors associated with cleft lip and palate birth defects in Jordan: A retrospective case-controlled study

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ABSTRACT

Aim: The study investigated the role of different factors could increase the potential risk factors of children with cleft lip and palate defects in the Jordanian population. *Materials and Methods:* Design: A case-control study where questionnaire used to assess different variables including environmental and medical factors. Setting: online questionnaire sent to mothers of children visiting Al-Karak Hospital, AL- Bashir Hospital and some charities delivering services to Children with CL/P. Study Duration: the study started from January 2021 and concluded in January 2022. Participants: questionnaire was answered by 100 mothers of children suffered CL/P (case group), and by 100 mothers of healthy children (control group). *Results:* The results were analysed in relation to the relative risk of each variable in order to estimate the odds ratio with a confidence interval of 95%. The analyses revealed that: family history of CL/P (OR= 4.91), Consanguinity marriage (OR= 3.29), previous illness of the mother (OR= 2.45), and maternal smoking (OR=1.09) are significantly increased risk factors for cleft lip or palate. However, the effect of taking folic acid or multivitamins showed no significant differences (OR= 0.68, p = 0.24). *Conclusion:* Risk factors associated with CL/P in the studied population are almost the same with those described in the previous related studies. Therefore, this study advised all healthcare givers to educate the public about these factors as the same factors related to other congenital problems.

Keywords: Cleft lip, cleft palate, risk factor, Jordan, consanguinity, maternal smoking, case-control study.

1. INTRODUCTION

Cleft lip in conjunction with cleft palate or cleft lip and palate is the most common orofacial congenital malformation found among live births, this sentence mentioned in various studies confirming its widespread (Alfwaress

et al., 2017a; De Biasi et al., 2014; Shaw et al., 2006). The risk factors also being discussed in many studies as well (Cheshmi et al., 2020; Jia et al., 2011; Leite and Koifman, 2009). However, these factors differ between studies (Sabbagh et al., 2014). Therefore, this study is conducted to investigate the role of some environmental and medical conditions as possible causative risk factors to giving birth to a child with malformations, especially with a Cleft Lip and/ or Palate. The prevalence rate of patients with CL/P in Jordan was reported between 1.39/1000 (Al Omari and Al-Omari, 2004) and 2.4/ 1000 (Aqrabawi, 2008). A recent Jordanian study focus on the “demographical characteristics, health status, and associated communication disorders in patients with orofacial clefts (OFCs) in Northern Jordan” stated that the prevalence is 1.3/1000 live births in northern Jordan (Alfwaress et al., 2017a) .

The scarceness of the Jordanian studies, in particular studies focus on other regions in Jordan, trigger the need of more research. Therefore, the purpose of our study is to increase the awareness of risk factors that associated with incident of CL/P anomalies, so that might decrease the prevalence of such anomalies in the upcoming generation. Increase the awareness of causes not only decrease the prevalence of cases but also decrease the financial burden of the lifelong reconstruction and or plastic surgeries, moreover the need of patients with CL/P to speech rehabilitation (Alfwaress et al., 2017a). This study investigated a new sample of patients and highlights the need of recent and comprehensive studies covering all regions to measure the prevalence of CL/P in Jordan and the associated factors and put measures to be taken by decision makers and health providers.

In Alfwaress et al., study (2017a) stated that families with poor socioeconomic status and lower education level are more likely to delay the treatment of their children with CL/P. Therefore, it may be instructive in this context to mention the role of social solidarity in the community which is represented by the charities work and donations to offer these surgeries in the lowest cost as could as possible. But it is not enough these days, as our country has a special role in hosting refugees from the entire Arab world, recently a Syrian refugee, this has imposed heavy burdens on individuals, families, communities, and nations. So many children have to wait for their surgeries while suffering from the complications and on the top is the psychological one, until their low-income families become able to afford their lifelong operations.

A high percentage of the CL/P in Jordan, with different nationalities, refugees, almost with no insurance and high level of poverty is the factors. This paper is a gentle call to draw the attention of international medical aid to those patients in need to urgent medical treatment.

2. METHODOLOGY

The study type is a case-control research, which benefitted of a retrospective data to investigate the role of different factors leading or could increase the potential of giving birth to children with CL/P. The study started from January 2021 by recruiting mothers of children suffering from the cleft lip and/or palate, and accomplished in January 2022. The study carried out in Jordan. Due to COVID-19 restriction protocols in Jordan, participants were allocated from patients visiting the second author as well as from a charity called "Atfaluna" who provide collaborations between the health care providers of such operations to low -income families who cannot afford it. A structured questionnaire was designed and approved by experienced authors. The questionnaire had been written in Arabic The questionnaire filled by third and fourth author after phone calling the mothers.

Questionnaire

The questionnaire was made up of two measures: demographical data and environmental and medical variables. The questionnaire is available upon request. In first part data such as: Mother and father's age, residency, mother's education level, the nature of the mother work, type of CL/P, the order of the child in his family (First, Mid and Last), the maternal age, consanguinity, similar family history, other congenital anomalies in the child, the psychological state of mother at the maternal period and a previous history of abortion or ectopic pregnancy or a preterm birth, and the gestation period were investigated. While the second part focused on the environmental and medical potential risk factors based on previous literatures (Alfwaress et al., 2017a; Sabbagh et al., 2014), such as: smoking, obesity, medical conditions and taking some medicine and vitamins, economical and mental status. As we have participants who have come from Syria, question about their war experiences, which is surely have a catastrophic effect on the health. Child's name and parents contacts details were taken for authors' future references.

Questionnaire was composed, approved, and statistically validated by experienced authors. It is worth to mention that the questions were in Arabic language then the answers translated and transferred to excel sheets for statistical analyses. Before collected the data the aim of the research was explained to participants. All mothers were consented orally and other available contacts' tool either WhatsApp or Facebook messengers. All the data are taken from the mothers of those children themselves and all other relatives' or any third-party answers were rejected, as we want to get a precise date from a person who is the mostly related to the child and his condition with no bias or misleading answers.

Patients and participants

Sample size calculated using online tool, epitool®, (Shaw et al., 2006) with expected OR of 5 and p value =0.05 the size per group should be 67 person as a minimum. Therefore, two hundred mothers were recruited to this study. The participants were divided into two equal groups: 100 mothers of children with CL/P (case group), and 100 mothers of children have no congenital abnormalities (control group). Children with CL/P were treated in Al-Karak Hospital and in AL Bashir, Hospital visiting the second author for consultation and treatments and some of them have done their operations via the pervious mentioned charity. The second group (control group) recruited by the third and fourth author through trusted social media groups. For confirmation, written informed consent was obtained from all participants, and the study was carried out with the approval of the Human Research Ethics Committee of the University number 232021

Statistical analysis

IBM SPSS Statistics version 28 was used to perform the statistical analysis in this study. Descriptive analysis performed. As this is a case-control study Chi-square test, relative risk and Odd Ratio were performed. Values of $p \leq 0.05$ were considered significant in this analysis.

3. RESULTS

Cleft distribution by type and classification is shown in (chart 1). The most common types of CL/P were median cleft palate and unilateral harelip and unilateral incomplete harelip ($n = 17$ each), followed by median cleft palate and cleft uvula 15 and 14 respectively. The demographical distributions of the studied sample displayed in Table 1.

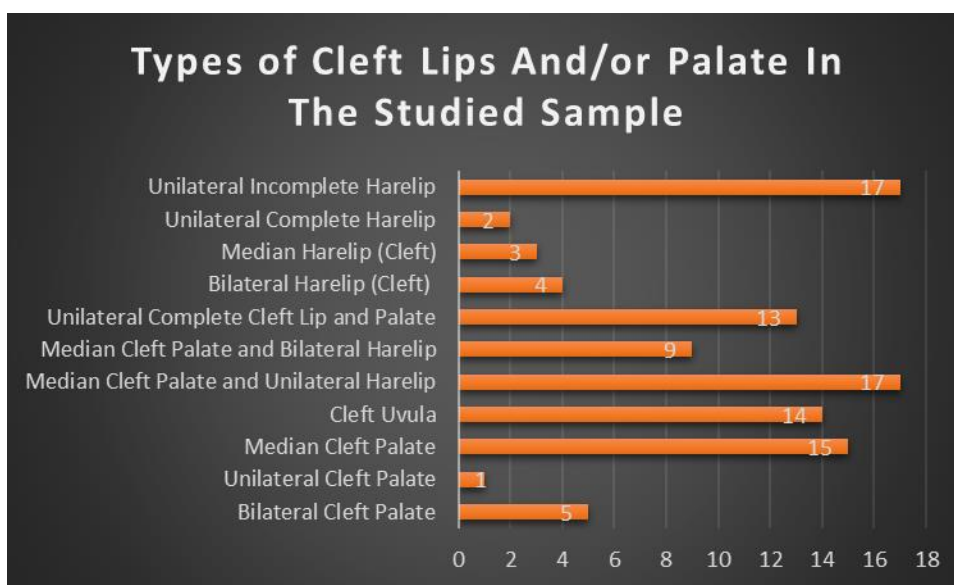


Chart 1 Type of Cleft Lips and/or Palate in the Studied Sample

Table 1 demographical distribution of the studied sample in both case and control groups.

Characteristics		Case Group	Control Group
Nationality	Jordanian	76	78
	Syrian	19	20
	Palestinian	4	1
	Iraqi	1	1
Mother's Age	< 18	3	1
	18-24	33	20
	25-31	33	49
	32-38	24	24
	39-45	7	6

Mother's Education Level	Illterary	3	0
	Basic Education	18	3
	Intermediated School	28	1
	Secondary School (Twjihi)	29	34
	Undergraduated	25	61
	Post-Graduated	0	1
Child Sex	Male		49
	Female		51
Father's Age	< 18	0	0
	18-24	9	4
	25-31	33	23
	32-38	35	51
	39-45	17	20
	> 45	6	2
Residency	Agricultural Area	6	2
	Polluted City	1	19
	Uncrowded City	65	60
	Village	24	15
	Syrian Refugees Camp	3	4
	Palestenian Refugees Camp	1	0
Having Other Congentinal Problem	Yes	26	0
	No	74	100

The general and medical characteristics of mothers distributed in the case and control groups, and Crosstabs statistical tests to assess the risk of CL/P development are presented in Table 2. Among the 200 participating children, 101 (50.5%) were male and 99 (49.5%) were female (p = 0.67). It was clear that some factors show significantly increased risk factors: smoking, obesity, consanguinity, family history of CL/P, and having a previous illness. Other factors, such as gender, or being a working mother were not statistically significant. Thorough statistical analysis on drugs: antihypertensive, diabetics', vitamins, folic acids, analgesics, contraceptive drugs, duphaston, and baby aspirin showed no significant results (p= 0.18- 0.66) or any correlation therefor no tables were displayed.

Table 2 General and medical characteristics of the mothers in both the case and the control groups, and multivariate analysis to assess the risk of CLP* development.

Characteristics	Case		Control		Total		OR	IC-95%	P VALUE
	number	%	number	%	number	%			
SEX									
MALE	49	24.5%	52	26.0%	101	50.5%	0.89	0.51-1.5	0.67
FEMALE	51	25.5%	48	24.0%	99	49.5%			
SMOKING									
YES	13	6.5%	12	6.0%	25	12.5%	1.09	0.47-2.54	0.00
NO	87	43.5%	88	44.0%	175	87.5%			
OBESITY									
YES	18	9.0%	18	9.0%	36	18%	1.00	0.47-	0.00

NO	82	41.0%	82	41.0%	164	82.0%		2.06	
FOLIC ACID/MULTIVITAMINS INTAKE									
YES	20	10.0%	27	13.5%	47	23.5%	0.68	0.35-	0.24
NO	80	40.0%	73	36.5%	153	76.5%		1.31	
CONSANGUINEOUS MARRIAGE									
YES	42	21.0%	18	9.0%	60	30.0%	3.29	1.73-	< 0.001
NO	58	29.0%	82	41.0%	140	70.0%		6.29	
PREVIOUS ILLNESS									
YES	45	22.5%	25	12.5%	70	35.0%	2.45	1.35-	0.003
NO	55	27.5%	75	37.5%	130	65.0%		4.47	
FAMILY HISTORY OF CLP									
YES	27	13.5%	7	3.5%	34	17.0%	4.91	2.02-	< 0.001
NO	73	36.5%	93	46.5%	166	83.0%		11.92	

*CLP: cleft lip and/or palate

4. DISCUSSION

This is a case-control study performed in University of Mutah recruiting patients treated at Alkarak government hospital and at AL Bashir Hospital from different Arabic nationality: Jordanian, Syrian, Palestinian, and Iraqi. This is a first study focus in population in Southern Jordan as previous studies focus in Northern Jordanian (Al Omari and Al-Omari, 2004; Alfwaress et al., 2017b; Aqrabawi, 2008; Rawashdeh and Jawdat Abu-Hawas, 2008). Neither of the Jordanian studies discussed the potential risk factors of CL/P. Many variables were analysed in this study including maternal and paternal age, mother’s education, residency, medical condition, previous pregnancies experience and problems. A thorough statistical analysis had been done. The following factors showed statistically significant results: Family history of CL/P recorded a higher score as a possible risk factor, OR=4.91. The results agree with previous studies such as (Leite and Koifman, 2009), that confirmed that the history of CL/P in the family of one parent or both of them was strongly associated with CL/P. Second important factor with OR=3.29 and a very strong p value < 0.00 was when parents are relative or a consanguineous marriage. This factor is also related to previous factor as being relative and having family history, which represents 15% in our sample “MAY” increase the potential of having other children with CL/P. Consanguinity is part of Arab costume and mentioned and confirmed in other Arabic studies as a risk factor (Alamoudi et al., 2014; Ravichandran et al., 2012; Sabbagh et al., 2015; Saeed et al., 2019); this risk factor also cited as a strong risk factor in other studies: Brazilian studies (da Silva and Sant’ Anna, 2013) and Chinese(Yao et al., 2011).

Maternal health is of no doubt important of her health and the baby. In this study, having a history of some diseases such as: diabetes, hypertension, thyroid gland problems increased the odd ratio OR= 2.45 of having babies with CL/P (Acuña-González et al., 2011). Smoking either passive (Jia et al., 2011) or active smoking (Angulo-Castro et al., 2017; Honein et al., 2007) declared as an environmental risk factor though in this study the OR is not that high (1.09) still it shows a significant result.

A study by Shaw et al., (2006) stated the importance of the nutrient such as folic acids and iron. The study recommended the intakes of iron and riboflavin to reduce CL/P. Other study by Itikala et al., (2001) recommended the intake of multivitamin; however, in this study more than 90% of the mothers in both groups claimed they took folic acids and vitamins during pregnancy. Therefore, it was not possible to detect any link between minerals intake and CL/P. One of the notifying results is that 26% of the studied sample acknowledged that their children have other congenital abnormality mainly related to the heart.

5. CONCLUSION

Risk factors associated with Cleft lip or palate patients in our study are almost the same factors described in the previous related studies. Therefore, it is recommended to educate people in the marriage ages to be aware of these risk factors to lessen the numbers of children suffering from these congenital anomalies.

Author Contributions

Amal Albitoosh: Conceptualization, drafting, and writing the final paper, corresponding author.

Saleh Abu Alhaj: data collection and supervision

Maryam Abutouq: design the questionnaire and distributed it

Forat Almaitah: design the questionnaire and distributed it

Lina Al-Shadfan: data collection

Youssef Hussein: supervision

Ashraf A. Zaghloul: methodology and statistical analysis.

Abulmaaty M. Elsayed: methodology and statistical analysis.

Mohammad Al-Zubi: proofreading and approve the final version.

Hussein Youssef: proofreading and approve the final version.

Ethical approval

The study was approved by the Medical Ethics Committee of Human Research Ethics Committee of the University Ethical approval code number 232021.

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Conflicts of interest

The authors declare that there are no conflicts of interests.

Data and materials availability

All data associated with this study are present in the paper.

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