

# The role of different factors in the development of cleft lip, palate, or both

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## Abstract

**Background:** Cleft lip and cleft palate refer to congenital malformations characterized by fissures or divisions in the upper lip, the palatal region of the mouth, or both. Cleft lip and cleft palate occur due to incomplete closure of face tissues during fetal development.

**Objective:** To identify the primary elements that could contribute to the occurrence of cleft lip and palate.

**Materials and Methods:** The sample included 1080 patients distributed between cleft lip only, cleft palate only, and cleft lip and palate. Parents of participants answered questions related to their medical and exposure history. Subjects were seen over 13 years, from 1 January 2010 to 31 December 2022. Participants came to our hospital with ages from a few hours to 3 months.

**Results:** The distribution of cleft types in the sample was as follows: 11.6% had cleft lip alone, 29.5% had cleft palate exclusively, and 57.3% had both cleft lip and palate. The most significant number of patients, 28%, were found to be first-born individuals. The majority of dads who exhibited patience were aged 30 years or older, accounting for 65% of the sample. Among these individuals, 8.6% had a concurrent systemic ailment, while 40% were identified as smokers. Most moms were between the age range of 16 to 30 years (65.4%). Incorporate additional factors into the analysis, including the presence of familial cleft history and psychiatric disorders.

**Conclusion:** We found a high frequency of consanguinity between the parents maternal psychology

factors such as fear, hearing bad news or hearing loud sounds like gunshots (prevalent during civilian war in Iraq between 2010-2014 years) among parents of children born with cleft lip and palate.

**Keywords:** Alternative medicine, Cytotoxicity, Plant extract, *Aristolochia cymbifera*, Oral medicine.

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## Introduction

Cleft lip and cleft palate are among the most common birth disorders and are inheritable conditions that can be part of a syndrome (1-5). Multiple genes and genetic mechanisms (6-11) as well as some teratogens and

maternal illnesses have been associated with clefts (13-23). Clefts can be associated with defects of the central nervous system, eyes, heart, muscle-skeleton, genitalia, abdomen, ears, thorax, endocrine system and skin (24). The aim of this

work was to identify risk factor for clefts relevant to the studied population.

## Materials and Methods

The sample of this study included 1080 patients (592 males and 488 females) who

came to Al-wasity hospital as they are referred from different areas. We studied all clefts born between 1 January 2010 to 31 December 2022, and children were a few hours to 3 months of age. Parents were asked to fill out a questionnaire and a clinical examination was done for recording the type of cleft.

The comprehensive assessment of a patient often encompasses a clinical examination, consisting of both extraoral and intraoral examinations. Following this examination, relevant information is recorded, and a case sheet is completed, which involves

addressing key inquiries of utmost significance. The categorization of abnormalities includes cleft lip, full cleft palate, soft palate cleft, and cleft lip and palate. The inquiries pertain to details such as name, age, residence, and the number of siblings they have. Additionally, there are queries on the health state of their father, including if he smokes, his educational background, the presence of chronic illnesses, and any medications he may be taking. For mother same question in addition to

- 1- Psychological problem during first 12 weeks

like stress, fairness, and any violence

- 2- If she affected by disease during first 12 weeks
- 3- If she takes medication and type of these drugs
- 4- Any history of apportion.

Finally, we record family history of clefts.

## Results

**Table 1** shows the frequency of each cleft type by sex:

<b><i>Type of cleft lip and palate</i></b>	<b><i>male</i></b>	<b><i>Female</i></b>
<b><i>Bilateral cleft lip</i></b>	<b><i>4</i></b>	<b><i>9</i></b>
<b><i>Unilateral cleft lip</i></b>	<b><i>75</i></b>	<b><i>53</i></b>
<b><i>Left unilateral cleft lip</i></b>	<b><i>42</i></b>	<b><i>38</i></b>
<b><i>Right unilateral cleft lip</i></b>	<b><i>33</i></b>	<b><i>15</i></b>
<b><i>Complete cleft palate</i></b>	<b><i>169</i></b>	<b><i>150</i></b>
<b><i>Cleft soft palate</i></b>	<b><i>20</i></b>	<b><i>9</i></b>
<b><i>Cleft lip and palate</i></b>	<b><i>324</i></b>	<b><i>295</i></b>
<b><i>Bilateral cleft lip and palate</i></b>	<b><i>120</i></b>	<b><i>90</i></b>
<b><i>Left unilateral cleft lip and palate</i></b>	<b><i>131</i></b>	<b><i>95</i></b>
<b><i>Right unilateral cleft lip and palate</i></b>	<b><i>73</i></b>	<b><i>110</i></b>

**The father:** Among fathers of children born with clefts, approximately 65% (702 individuals) of fathers aged above 30 years age, 8.61% of these fathers (93 individuals) had been diagnosed with systemic diseases. The majority of these fathers (81%, 875 individuals) were employed in the free enterprise sector, while the remaining individuals worked in civilian and non-civilian occupations. The systemic diseases observed in these fathers include hypertension, diabetes, anemia, hormonal disorders, and others. Additionally, 40.6% of these fathers are smokers, and 2% consume alcohol.

**Mother:** The study revealed that a significant proportion of mothers, namely 65.4% (n = 706), fell between the age range of 20 to 30 years. Furthermore, a substantial majority of mothers, accounting for 90% (n = 972), were identified as housewives. Among these housewives, 70% (n = 756) were discovered to possess a poor level of

education. In the study, it was found that 80.6% (n=870) of women had normal births, whilst 19.4% (n=210) underwent cesarean operations. Furthermore, it was found that 19.8% (n=216) of the surveyed mothers had a documented history of undergoing abortion procedures. Among this group, 20% (n=216) had experienced repeated instances of abortion.

**Consanguinity:** The study revealed that the degree of consanguinity among the parents was determined to be 71% (N=767). The researchers acquired information about the occurrence of clefts within the nuclear family unit, which includes the father, mother, and siblings. The prevalence of clefts within this family was found to be 10%. There were two sets of male and female twins, all of them had cleft lip and palate at an identical location. All individuals with a familial predisposition to cleft lip and palate had full clefts, which were seen to be either unilateral or bilateral. During

the first trimester of pregnancy, a significant proportion of mothers, namely 39.2%, experienced the presence of illnesses. The most frequent conditions were shown to be urinary tract infections, anemia, respiratory illnesses, and hypertension... During the first trimester of pregnancy, a significant proportion of mothers, namely 40% or 432 individuals, reported the use of various medicines including antibiotics, vitamins, insulin, anti-inflammatory drugs, steroids, and contraceptive pills, among others.

**Psychological role in cleft development:** 46.6% of mothers reported fear, hearing bad news or hearing loud sounds like gunshots. 6% of mothers had a history of physical trauma. Most events were concentrated between the years 2010 to 2014 where there was military action in most of Iraq.

When taking the order of birth of the affected child, 32.12%, or 347 were first born.

**Table 2** shows the frequency of associations with other congenital anomalies:

System affected	percentage	
Craniofacial	3.8	41
Central Nervous System	1.57	17
Ocular	0.64	7
Cardiac	2.6	28
Urogenital	1.2	13
Musculoskeletal system	3.61	39
Ear	1.48	16

## Discussion

In this research, the prevalence of cleft lip was seen to be lower (11.6%) compared to other types, which is consistent with the findings of previous studies such as Kinaan (15%), Al-Zubaidee and Hammash (16.67%), and Dawood (15%) (21-23). However, a significant difference was seen among the other investigations conducted by Natsume and Kawai (2013) (41.3%), Manhal (2012) (10%), and Al-Zubaidee et al. (1998) (50%) in their respective findings. A previous study by Manhal (24), Al-Zubaidee, and Hammash (22) indicated that the frequency of unilateral clefts was greater than that of bilateral clefts.. The findings of this research also revealed a prevalence of left-sided clefts, which accounted for a greater

proportion than right-sided clefts across all kinds of cleft lip instances. This phenomenon might perhaps be attributed to the rotation of the head towards the right during the embryonic development of the heart, resulting in the inferior positioning of the left side of the face. In the instance of cleft palate, the prevalence rate of 29.5% was observed, which was somewhat lower compared to the findings reported by Sesgin and Stark (33%), Conway and Wagner (32%), Padilla and Gonzalez (1986) (33.1%), Dawood (1997) (33%), and Al-Zubaidee et al. (2000) (38%). The occurrence of cleft of the soft palate was comparatively less frequent as compared to that of the hard palate. Borcbakan (1969) documented a greater prevalence of clefts occurring in the soft palate

compared to those occurring in the hard palate. Cleft lip and palate, also known as orofacial clefts, are congenital conditions characterized by a separation or gap in the upper lip and/or the roof of the mouth. The aforementioned group constituted the majority of various forms Previous investigations have shown the occurrence of cleft, with Manhal (21-25) reporting a prevalence rate of 67%, Dawood (23) reporting a rate of 52.14%, and Al-Zubaidee (22) reporting a rate of 45%. The research conducted in this study revealed a more significant occurrence of unilateral cleft lip and palate compared to bilateral cleft lip and palate, which aligns with the findings provided by Dawood (23). However, these results differ from those

obtained by Manhal (24). The individual in question, referred to as Kinaan (21), is the subject of discussion. The examination revealed a lack of occurrences of median cleft lip and palate, a facial abnormality that is seldom seen and has been hardly documented in previous studies, including the research conducted by Manhal (24). Dawood (2019) discovered a specific form of median cleft in a subset of individuals, constituting around 1.07% of the population. When considering the impact of sex, it is seen that males are impacted to a greater extent than females, with a ratio of 1.2:1. Specifically, a study conducted by Manhal (24) found a slightly higher ratio of 1.27:1. The sexual dimorphism in the prevalence of clefts remains uncertain; nonetheless, it has been postulated that divergent morphogenic processes in facial development between males and females may underlie this disparity.. Upon examination of the fathers' age, it was noted that there was a greater incidence of cleft in the older age cohort. Nevertheless, Jensen et al. (1988) documented a somewhat elevated incidence of cleft births in cases when the fathers

were below the age of 24, which contrasts with the relationship between maternal age and cleft occurrence. Specifically, it was found that approximately 65.4% of cleft patients were born to younger mothers aged between 14 and 30 years old. This finding aligns with the research conducted by Manhal (24). According to Slavkin (1992), research conducted by Fraser and Calnan (1961) discovered a positive correlation between the incidence of mouth clefts and advanced maternal age. This research reveals that a significant proportion of parents, namely 71%, exhibit a familial relationship. This finding aligns with the findings of Dawood (23). The prevalence of family history, as reported by Pietrzyk et al. (1985), was found to be consistent with the findings of the current study in 10% of cases. AL-Zubaidee et al. (2000)(22), on the other hand, found a lower rate of 6.8%. According to Dawood (23), a study found that 39.2% of women experienced illnesses during the first trimester of their pregnancy. Additionally, the study reported that 36.3% of moms had a condition during this period. Several studies have identified certain diseases,

like epilepsy (Niebly, 12), diabetes (Nada, 1975), and Rubella (Seaver and Hoyer, 1992), as potential causes of cleft lip and palate.. A study conducted by Manhal (24) found that around 46.6% of moms experienced psychological distress. It is worth noting that this percentage falls within the range of 65% given by Manhal. Around 50.8% of children who get a diagnosis of either unilateral or bilateral cleft lip and palate need the use of a feeding plate, a medical intervention normally delivered by an orthodontist. In instances when there is a co-occurrence of defects in other organs, it has been shown that around 14.9% of patients exhibit conditions such as cranial abnormalities, intellectual disability, visual impairments, cardiac malformations, and urogenital abnormalities. The prevalence of related abnormalities in the musculoskeletal system and ear was found to be greater in the current research compared to a previous study conducted in Iran. The previous study had a sample size of 1669 patients with cleft lip and palate and reported a prevalence rate of around 7.73% for associated

anomalies. However, in research conducted in France (25), it was shown that the proportion was lower than 36.7%.

## Conclusions

- 1 The use of drugs during the first trimester of pregnancy has a crucial role in the occurrence of this particular kind of deformity.
- 2 In the sample, a positive consanguinity between the parents was observed in 71% of cases.
- 3 The research demonstrates the potential of psychological variables in influencing outcomes.

## Disclosure of interest

The authors declare that they have no competing interests.

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