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ORIGINAL PAPER

Cleft lip and palate in newborns: 17 years of institutional research and clinical experience

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ABSTRACT

Introduction: The aim of the study is to show the frequency and characteristics of newborns with cleft lip (CL), cleft palate (CP), and cleft lip and palate (CLP) and their mothers at our clinical center over a 17-year period.

Material and methods: A retrospective study was conducted in the period from January 2009 to December 2025 at the Department of Neonatology and the Department of Intensive Care for Children (Neonatal Intensive Care Unit) the Clinic for Children's Diseases of the University Clinical Hospital in Mostar. The study included 51 newborns and their mothers who were diagnosed with one of the orofacial clefts (CL, CP (hard and soft palate) and CLP) during pregnancy or after birth.

Results: Of the 29,544 infants born at the University Clinical Hospital in Mostar between January 1, 2009 and December 31, 2025, 51 newborns (0.17%) were treated for congenital orofacial clefts (CL, CP, CLP). In the last eight years of the study, 68.6% (35/51) of cases of CL, CP and CLP in newborns were recorded which is significantly higher than in the previous 9 years when 31.4% (16/51) of such newborns were recorded ($p = 0.008$). The results indicate a significant dominance of CL and hard and soft palate (22) and (17) cleft soft palate ($p = 0.002$), 39/51 newborns. In 24 of 51 newborns (47.1%), an orofacial cleft was detected during pregnancy. Isolated congenital orofacial clefts without other pathological conditions were present in 20 newborns, while 31 of them also had other pathological conditions and/or congenital anomalies of other organ systems ($p = 0.123$).

Conclusions: During the 17-year study, the incidence of oral cavity malformations (CL, CP, CLP) in newborns was low compared to the number of births at our clinical center. Nevertheless, we must not forget the importance of screening, diagnosing and monitoring pregnant women with such malformations in their newborns for better neonatal care and favorable treatment outcomes.

KEY WORDS:

cleft lip and palate, newborn, facial malformations.

INTRODUCTION

Orofacial clefts, such as cleft lip (CL), cleft palate (CP), and cleft lip and palate (CLP), are among the most common birth defects affecting the head and neck. They occur across all populations, ethnic groups, and socioeconomic strata [1]. The global prevalence of orofacial clefts varies according to geographical location and/or race [2]; in Europe, the prevalence ranges 1–2.21 per 1,000 newborns [3]. Both hereditary and environmental factors (e.g., medication, radiation, alcohol, and smoking) play a role in the development of orofacial cleft [2]. Possible associations between parental age, sex-based differences, educational attainment, and family income with the occurrence of orofacial clefts remain contradictory, highlighting the need for further research to gain deeper

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insights [4]. The observed upward trend in cleft cases is likely associated with socioeconomic factors, such as teenage pregnancies, advanced maternal age (over 35), and increased exposure to teratogens during the early stages of pregnancy [5]. Cleft lip, CP, and CLP are congenital defects characterized by a lack of tissue in the upper lip, alveolar ridge, and/or palate. Because the lip and palate form at different gestational stages, a child may be born with an isolated CL, an isolated CP, or a combined CLP. Several syndromes also have orofacial cleft as part of their clinical picture. Approximately 15% of all clefts are syndromic, of which approximately 50% are cases of an isolated CP [6]. As the causes and mechanisms of cleft development are not yet fully understood, their occurrence cannot be prevented. In developed countries, CL, CP, and CLP are usually identified prenatally through ultrasound screening. Early detection provides a critical window for parental education regarding the potential causes of CL, CP, and CLP, and the procedures the child may require postnatally. Even today, many clefts are first diagnosed at delivery. The birth of an infant with a CL, CP, or CLP can be profoundly distressing for parents, particularly in the absence of specialist support. Prenatal diagnosis enables parents to emotionally prepare for the arrival of a child with a cleft, ideally through consultation with neonatologists who specialize in postnatal care of newborns with clefts [7]. Families with a history of orofacial clefts, as well as affected individuals seeking to understand the recurrence risks for their offspring, should be referred to a genetic counseling clinic. Despite the localized nature of the malformation, the comprehensive management of clefts necessitates a team approach from birth until skeletal maturity. Treatment is long-term, extending until the completion of skeletal maturity; consequently, no single specialist can independently address all areas of treatment. Owing to the vast array of risk factors and the incomplete understanding of the mechanisms governing orofacial development, preventive measures to mitigate the occurrence of CL, CP, and CLP have yet to be fully established [8]. Therefore, the objective of this study is to delineate the prevalence and clinical characteristics of neonates with CL, CP, and CLP at our clinical center over a 17-year period.

MATERIAL AND METHODS

This retrospective cohort study was conducted at the Department of Neonatology and the Neonatal Intensive Care Unit (NICU) within the Clinic for Children's Diseases of the University Clinical Hospital (UCH) in Mostar, covering the period from January 1, 2009 to December 31, 2025. The study population comprised all pregnant women and their newborns residing permanently within the Herzegovina-Neretva and West Herzegovina Cantons, both of which constitute the primary catchment area for our clinical center. Data were retrieved from clinical protocols, transfer documentation, medical records, and neonatal discharge letters following the admission and treatment of infants at the Department of Neonatology and the NICU. The study comprised 51 neonates and their mothers; all infants were diagnosed with an orofacial cleft (CL, CP involving the hard and/or soft palate**,** or CLP) either prenatally or postnatally and received treatment at the Department of Neonatology and the NICU within the Clinic for Children's Diseases.

Cleft lip, CP, and CLP represent the most prevalent congenital head and neck malformations. They are characterized by a lack of anatomical structure involving the upper lip, the alveolar ridge, and the hard and/or soft palate. Cleft lip was colloquially referred to as a "hare lip," while CP or combined CL and palate was termed a "wolf's pharynx." The etiology of CL and/or cleft palate is complex, involving genetic predisposition and environmental factors. While the precise pathogenesis of CL and/or cleft palate remains elusive, it is thought to result from incomplete development of the lip and/or palate during facial development between the sixth and eighth gestational weeks. Because the lip and palate develop during distinct stages, clefts may involve the lip, the palate, or both. The study included all neonates presenting with isolated congenital malformations of the lip and palate, as well as those where the clefts occurred as a component of a clinical syndrome [1, 2].

Maternal parameters analyzed included age, parity, abortions, type of conception, mode of delivery, type of pregnancy, pregnancy complications (hemorrhage, placenta previa), pathological conditions in pregnancy as documented in the clinical discharge letters, medication, the timing of the cleft diagnosis, and course of pregnancy. Neonatal parameters included biological sex, age at transfer, gestational age, birth weight, birth length, head circumference, vitality assessment (Apgar score), referral diagnosis, discharge diagnosis, time to first tolerated feed, feeding method, orofacial cleft phenotype (CL, CP, CLP), categorized as either isolated or syndromic, consultation with maxillofacial surgeons, complications (hyperbilirubinemia, infection, sepsis), neuro-sonography, therapeutic interventions, duration of treatment, outcome, and other gestational pathological conditions as documented in their respective discharge letters. An ultrasound device (Versana Active 9, manufactured by GE Healthcare Ultrasound), available at the Clinic, was used for morphological brain imaging.

STATISTICAL METHODS

Statistical analysis was performed using IBM SPSS Statistics for Windows, Version 25.0 (IBM Corp., Armonk, NY, USA). The results are presented as absolute numbers and percentages. For testing differences in prevalence, the χ^2 test was used. The level of statistical significance was set at $\alpha = 0.005$. *P*-values are reported to three decimal places, and values lower than 0.001 are reported as $p < 0.001$.

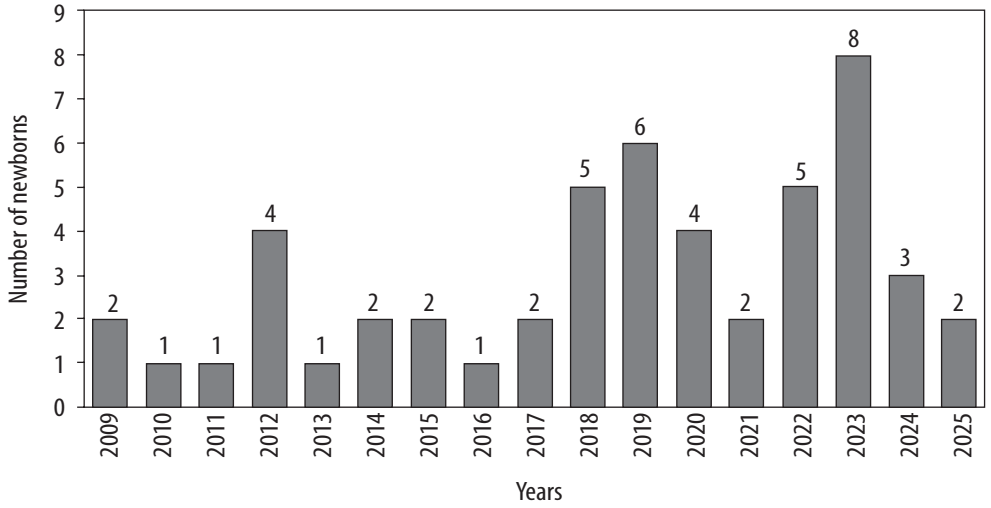

FIGURE 1. The distribution of newborns with orofacial clefts (cleft lip, cleft palate, and cleft lip and palate) identified throughout the study period

RESULTS

Of the 29,544 infants born at the UCH Mostar between January 1, 2009, and December 31, 2025, 51 newborns (0.17%) were treated for congenital orofacial clefts (CL, CP, CLP) at the Department of Neonatology and the NICU at the Clinic for Children's Diseases of the UCH. Of the 51 newborns, 4 (7.8%) were treated at the NICU for severe malformations. In all four cases, the clinical course resulted in a fatal outcome. The remaining 47 (92.1%) newborns were treated and processed at the Department of Neonatology. Our hospital has seen a decline in birth rates over the period, decreasing from approximately 2,500 annual deliveries in the inial years to a stable mean of 1,850 in later years, followed by an increase to nearly 2,000 births in 2024. The distribution of diagnoses among the 51 newborns was as follows: 22 (43.1%) presented with CL and 22 (43.1%) presented with CL and hard and soft palate involvement, 17 (33.3%) with a cleft soft palate, 6 (11.7%) with both hard and soft palate clefts, and 6 (11.7%) with CL only. The results indicate a significant dominance of CL and hard and soft palate (22) and (17) cleft soft palate ($p = 0.002$), 39/51 newborns.

TABLE 1. The maternal characteristics associated with newborns affected by orofacial clefts (cleft lip, cleft palate, and cleft lip and palate) throughout the study period

Parameters	Number of mothers	Percentage
Age at pregnancy		
20–30	25	49.0
31+	26	51.0
Mode of delivery		
Vaginal	35	68.6
Cesarean	16	31.4
Type of pregnancy		
Single pregnancy	50	98.0
Multiple pregnancy	1	2.0
Abortion		
No	45	88.2
Yes	6	11.8
Parity		
1	28	54.9
2	13	25.5
3+	10	19.6
Pregnancy course		
Normal	40	78.4
Pathological	11	21.6

Throughout the analysis period, an upward trend in orofacial cleft cases (CL, CP, CLP) was observed. While the frequency peaked in 2023, the number of cases decreased by more than 50% by 2025 (Figure 1). Significantly more CL/P cases occurred in the latter eight years of the study (68.6%, 35/51) compared to the previous nine years (31.4%, 16/51; $p = 0.008$).

During the initial nine years of the study (2009–2017), the incidence remained low, with typically 1–2 newborns recorded annually, except for a minor peak of four cases in 2012.

Mothers were distributed almost equally across age groups: 25 (49%) were younger than 30, while 26 (51%) were over 30 years of age. 35 (68.6%) of them gave birth by vaginal delivery. Only one case of multiple pregnancy was recorded, and most mothers had no prior abortions, more than half are primiparous (Table 1).

Female newborns were more frequent in the study population. Apgar scores were generally good at 1 and 5 minutes (Table 2). Over 50% of the newborns commenced feeding within the first day, while nine required nasogastric tube feeding (Table 2).

In 24 of 51 newborns, an orofacial cleft case (CL, CP, CLP) was detected during pregnancy. Six newborns had an orofacial cleft as part of the syndrome (Stickler, Pierre Robin and/or Patau syndrome). Of the 6, four were reported in mothers younger than 30 years of age, while

TABLE 2. The parameters of the newborns diagnosed with orofacial clefts (cleft lip, cleft palate, and cleft lip and palate) throughout the study period

Parameters	Number of newborns	Percentage
Gender		
Male	22	43.1
Female	29	56.9
Vitality score in first minute		
≤ 7	5	9.8
8–10	46	90.2
Vitality score in fifth minute		
≤ 7	3	5.9
8–10	48	94.1
Time of first feed orally [hours]		
0–24	29	56.9
25–72	8	15.7
> 72	14	27.4
Feeding method		
Specialized bottles	41	80.3
Through a nasogastric tube	10	19.6
Brain ultrasound at birth		
Normal	41	80.4
HIC 1	5	9.8
HIC 2	4	7.8
HIC 3	1	2.0

TABLE 3. Other characteristics of newborns with orofacial clefts and the prevalence of multiple congenital anomalies of other organ systems in newborns with orofacial clefts (cleft lip, cleft palate, and cleft lip and palate) during the study period

Parameters	Number of newborns	Percentage
Orofacial clefts detected during pregnancy		
Yes	24	47.1
No	27	52.9
Orofacial clefts as part of the syndrome		
Yes	6	11.8
No	45	88.2
Isolated orofacial clefts		
Yes	20	39.2
No	31	60.8
Congenital anomalies of other organ systems*		
Cardiac disorder	7	
Chromosomal disorder	5	
Extremity deformation	7	
Respiratory disorder	3	
Surgical anomaly	1	
Nephrological disorder	1	

** Some newborns had multiple congenital anomalies of other organ systems at the same time.*

two cases were reported in mothers older than 31 years of age. Prenatal diagnosis was performed in 6 cases where fetal malformation was suspected. Over 47% of cases of orofacial clefts (CL, CP, CLP) were diagnosed by prenatal ultrasound, especially in recent years of research.

Isolated orofacial clefts without other pathological conditions was present in 20 newborns, while 31 of them also had other pathological conditions and/or congenital anomalies of other organ systems ($p = 0.123$). Of these 31, 16 were recorded in newborns whose mothers were under 30 years old, and 15 in mothers over 30 years old. Among the congenital anomalies of other organ systems, heart disorders and limb deformities and chromosomal disorders were most often recorded, with some newborns having more than one of the anomalies listed in Table 3.

DISCUSSION

Facial malformations are structural anomalies that affect approximately 2–3% of the global population. They arise from diverse factors that impact the body and are visible at birth. They can also be detected during intrauterine life [9]. The prevalence of orofacial clefts (CL, CP, CLP) in our hospital was 1.7 per 1,000 live births during the 17-year study period, which mirrors the frequency observed in neighboring Croatia, where 70–80 children were born annually with orofacial clefts. Cross-country comparisons are hindered by the lack of a common registry of malformations. Therefore, data must be drawn from individual hospital departments and hospital registries [10]; this methodological approach was utilized in the present study. A notable upward trend in the prevalence of orofacial clefts (CL, CP, CLP) was observed during the COVID-19 pandemic at our clinical center. These findings align with a 2024 study, which suggests a potential correlation between maternal COVID-19 infection and the development of orofacial malformations [11]. Our observations also align with a 2025 study identifying exposure to stressful life events, such as fear of contracting the COVID-19 infection, as a potential trigger for non-syndromic orofacial clefts [12]. The highest incidence at our clinical center was attributed to combined CLP at 43.1%. These data are consistent with studies conducted in India, which similarly report a higher prevalence of CLP [13].

Global studies have documented variable prevalences of orofacial clefts, significantly influenced by ethnicity, sex, and orofacial cleft type. Epidemiological data and research findings indicate that the risk of occurrence is heightened by a combination of factors, such as a positive family history, advanced maternal age (> 35 years), pre-gestational diabetes, and hypertension [14]. At our

clinical center, the majority of deliveries were vaginal, a finding that contradicts a study indicating a higher incidence of cesarean sections as the mode of delivery for newborns with orofacial clefts (CL, CP, CLP) [15]. Our results indicate a relatively balanced distribution of maternal age with 51% of mothers aged 30 years and older. These results contrast with the prevailing clinical view that the risk of giving birth to children with orofacial clefts (CL, CP, CLP) increases with maternal age [16, 17]. Some factors, such as maternal infections, diabetes, and hypothyroidism, were also identified as risk factors in our study. However, our results regarding multiparity diverged from established trends. While previous research indicated that the odds ratio for CL, CP, CLP increases with the number of pregnancies [18], our findings did not demonstrate a significant parity-related risk. Our results show that 55% of the orofacial cleft cases (CL, CP, CLP) occurred in first-time, single pregnancies, with more than 88% of the mothers having no history of abortion in our study. While global studies have reported that orofacial clefts are more common in boys [10, 13], our study found a slightly higher prevalence in girls. Over 92% of the newborns had normal Apgar scores, which suggests that the anomaly itself did not significantly affect post-delivery vitality at our clinical center.

Most developed countries now identify orofacial clefts before birth using ultrasound screening. However, a study conducted in Denmark shows that before 2005, clefts were rarely diagnosed intrauterinely, while in recent years, failure to diagnose clefts intrauterinely is very rare [19]. Which is similar to our results. Over 50% of CL or CP cases were diagnosed at birth, especially in the first ten years of the study. The undiagnosed cases were most likely due to several factors such as irregular gynecological follow-ups, limited ultrasound resolution, and the inherent technical difficulty of visualizing certain anomalies – particularly isolated palatal clefts. Furthermore, during the early stages of the study, less extensive experience in screening for these relatively rare malformations may have also contributed to lower detection rates. In recent years, expectant mothers have undergone regular prenatal monitoring by specialized gynecologists.

Approximately 70% of CL and CLP cases and 50% of CP cases are considered non-syndromic, presenting as an isolated anomaly without other structural disturbances [20]. In our study, only 11.7% of the newborns had orofacial clefts associated with a known clinical syndrome. Our findings are consistent with those of other studies, which indicate that approximately 15% of all orofacial clefts occur in association with a clinical syndrome [21], and in 50% of these syndromic cases, they present as isolated CP [22]. Syndromes in our study were verified through cytogenetic analysis. At our clinical center, termination of pregnancy is a legally available option. While expectant mothers diagnosed with severe fetal malformations during the first trimester are informed of the possibility of termination, the refusal rate in our area is notably high. These decisions are frequently influenced by strong religious convictions, leading most women to proceed with the birth even when a severe anomaly has been confirmed. During the course of neonatal intensive care, a fatal outcome occurred in four newborns.

Orofacial clefts complicate an infant's life from birth. Because of the many associated pathological conditions found in these newborns, a multidisciplinary team including maxillofacial surgeons, geneticists, and pediatric subspecialists is required to address the complex needs of infants with orofacial clefts (CL, CP, CLP). Therefore, effective monitoring and prenatal verification of orofacial clefts (CL, CP, CLP) are vital for ensuring immediate access to neonatal care. Learning the diagnosis before birth significantly reduces maternal stress, fear, and guilt. This preparation is crucial because newborns with orofacial clefts (CL, CP, CLP) are often transferred to other facilities for specialized care, and early diagnosis helps mothers cope with the emotional impact of their early separation [23]. The burden of care falls largely on neonatologists, who must demonstrate high-level skills in clinical management and communicating with concerned parents.

A primary limitation of this study is the absence of a national cleft registry for every hospital in our country, which precludes the calculation of a definitive nationwide incidence. Consequently, our findings reflect the institutional frequency of orofacial clefts within a clinical center serving two cantons.

CONCLUSIONS

Our clinical center observed a low incidence of oral cavity malformations (CL, CP, CLP) in newborns relative to total births over a 17-year period. However, the importance of early detection through maternal screening and monitoring remains paramount. Accurate prenatal diagnosis is the cornerstone of effective neonatal care and is vital for ensuring the best possible recovery and treatment outcomes.

DISCLOSURES

1. Institutional review board statement: This study was approved by the Ethics Committee of the School of Medicine of the University of Mostar (approval decision no. 01-I 287/24, dated 14.05.2024).
2. Assistance with the article: None.
3. Financial support and sponsorship: None.
4. Conflicts of interest: None.

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