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Congenital Cardiac Anomalies in Children with Cleft Lips and/or Palates in Yaounde: A Cross-Sectional Retrospective Study

Malformations congénitales cardiaques dans une population pédiatrique de porteurs de fentes labiopalatines à Yaoundé : une étude transversale rétrospective

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HIGHLIGHTS

What is already known on this topic
In addition to the aesthetic problem and the negative impact on psychomotor development that they may cause, cleft palates (CP) may be associated with other congenital heart diseases. However, this has not been studied in Cameroon.

What question this study addressed
Frequency and sonographic presentation of congenital heart diseases in children with CP in Yaounde.

What this study adds to our knowledge
The prevalence of congenital heart defects in children with cleft palate in Cameroon is high. These are mainly atrial septal defect and patent ductus arteriosus.

How this is relevant to practice, policy or further research.
Cardiac evaluation of these patients is necessary to identify potentially high risk patients.

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ABSTRACT

Introduction. Cleft palate are frequently associated with other congenital malformations, particularly cardiac ones, impacting the overall management of patients. There are no data in our setting on the association of cleft palate with congenital heart defects. **Methods**. We carried out a cross-sectional analytical study with retrospective and prospective data collection during a period of five years, at the Yaounde Gynaeco-Obstetric and Paediatric Hospital. All patients under 18 years of age who consulted for cleft palate were included in our study. **Results**. We enrolled 76 patients. The median age was 3 months with an interquartile range of [2-6] months. Primary cleft palate was found in 42 patients (55.26%), secondary cleft palate in 4 patients (5.26%) and primary and secondary cleft palate in 30 patients (39.47%). A congenital heart defect was found in 20 of the 76 patients (26.32%). All cardiopathies were simple and non-cyanogenic. The most common was atrial septal defect (17.10%) followed by patent ductus arteriosus (5.26%). There was no significant association between the type of cleft and the type of cardiac anomaly. **Conclusion**. The prevalence of congenital heart defects in children with cleft palate in Cameroon is high. Cardiac evaluation of these patients is necessary to identify potentially high risk patients.

RÉSUMÉ

Introduction. Les fentes labiopalatines fréquemment associées à d'autres malformations congénitales, notamment celles cardiaques, impactent la prise en charge globale des patients. Il n'existe pas de données dans notre milieu quant à l'association fentes labiopalatines et anomalies cardiaques congénitales. **Méthodologie**. Nous avons mené une étude transversale analytique à collecte de données rétrospective et prospective sur une période de cinq ans, à l'Hôpital Gynéco-Obstétrique et Pédiatrique de Yaoundé. Etaient inclus dans notre étude, tout patient âgé de moins de 18 ans ayant consulté dans cette formation sanitaire pour fente labiopalatine. **Résultats**. Nous avons recruté 76 patients. L'âge médian était de 3 mois avec un intervalle interquartile de [2-6] mois. On retrouvait les fentes du palais primaire chez 42 patients (55,26%), les fentes du palais secondaire chez 4 patients (5,26%) et les fentes des palais primaire et secondaire chez 30 patients (39,47%). Une anomalie cardiaque congénitale était retrouvée chez 26,32%. Parmi ces cardiopathies, toutes étaient simples et non cyanogènes. La plus retrouvée était la communication inter auriculaire (17,10%), suivie de la persistance du canal artériel (5.26%). Nous n'avons pas retrouvé d'association significative entre le type de fente et le type d'anomalie cardiaque. **Conclusion**. La prévalence des anomalies cardiaques congénitales chez les enfants porteurs de fentes labiopalatines au Cameroun est élevée. L'évaluation de ces patients sur le plan cardiaque est nécessaire pour identifier les patients potentiellement à haut risque.

INTRODUCTION

Cleft lip and palate are congenital malformations whose prevalence is estimated by the WHO to be 1 per 1200 births in Africa [1]. Cleft lip and palate are divided anatomically into primary cleft palate (PCP), secondary cleft palate (SCP), and primary and secondary cleft palate (PSG), although other classifications exist. In addition to the aesthetic problem and the negative impact on psychomotor development that they may cause, cleft palates may be associated with other congenital malformations, notably cardiac [2]. It is therefore essential for the management of patients to first investigate the presence of another associated cardiac malformation in order to guarantee a personalized management. This would avoid additional costs and ensure a better therapeutic sequence. There is no data on this association in the Cameroonian literature, which is why we propose to study it in our context. The aim was to describe the clinical and echocardiographic aspects found in children with cleft lip and palate in the city of Yaoundé.

METHODS

We conducted a retrospective and prospective cross-sectional analytic study at the Yaoundé Gyneco-Obstetric and Pediatric Hospital from January 1, 2017, to May 1, 2022, on patients who consulted this health facility for cleft lip and palate. The inclusion and exclusion criteria were as follows:

Inclusion criteria:

- Patients under 18 years of age
- Cleft lip and palate patients
- Having performed a cardiac ultrasound and with a complete report

Exclusion criteria:

- Patients of foreign nationality
- Patients whose parents did not consent to participate in the prospective phase of the study.

Our variables of interest were the following: age at the time of the echocardiogram, sex, personal and family history, type of cleft observed, dysmorphia and syndromes found, elements of the cardiac physical examination, and data from the echocardiogram report. These data were entered into a questionnaire designed for this study.

Our study protocol was approved by the Institutional Ethics and Research Committee of the Faculty of Medicine and Biomedical Sciences of the University of Yaoundé I (N°169/UYI/FMSB/VDRC/CSD) and the Institutional Ethics and Research Committee in Human Sciences of the Yaoundé Gyneco-Obstetric and Pediatric Hospital (170/CIERSH/DM/2022).

Our sampling was consecutive and non-probability. Data were analyzed using SPSS 23.0 software and expressed in terms of frequency, median and interquartile range. Chi-square and Fisher tests were used in the association calculations, and a P value ≤ 0.05 was considered statistically significant.

RESULTS

A total of 139 patients with cleft lip and palate were seen over the study period. However, only 76 of them had complete data and were included in our study.

The median age was 3 months with an interquartile range of [2-6] months. Girls were the most represented, representing 65.8% of our study population; with a M/F sex ratio of 0.52 (table I).

Regarding the past medical history, we found 2.7% of patients whose mothers used tobacco and 18.4% of patients whose mothers used alcohol during pregnancy. Remaining in this chapter, fever during the first trimester of pregnancy was found in 11% of patients.

As another antecedent, the unexplained death of an infant or young adult in the first degree was noted in 5.2% of patients. In our study population, 7.9% of patients had another associated malformation and 2/3 of them were girls. Limb defects accounted for 66.7% of these patients and renal defects for 33.3% (table I).

Table I : General characteristics of the study population.

	N	
Age		
< 28 days	8	10,5
[29 days - 3 months [	20	26,3
[3 months – 6 months [	28	36,9
[6 months - 1 year[	8	10,5
> 1 year	12	15,8
Sex		
Male	26	34,2
Female	50	65,8
Past history		
Tobacco in pregnancy (Yes/No	2 / 76	2,7 / 97,3
Alcohol in pregnancy (Yes/No)	14 / 62	18,4 / 81,6
T1 fever (Yes/No)	8 / 68	11 / 89
Unexplained death in infant or young adult 1st degree	4 / 72	5,2 / 94,8
Auxiliary malformation		
Limbs (Polydactyly)	4	5,2
Renal (Single kidney)	2	2,7
None	70	92,1

T1 = first trimester in pregnancy

Clefts of the primary palate were found in 55.3% of patients. Of these, 39.5% had an isolated cleft lip (FL) while none had an exclusive cleft alveolar (FA).

The primary and secondary cleft palate group represented 39.5% of our study population. In this group, 1 in 3 patients was male. Secondary cleft palates were the least represented in our series with a proportion of 5.2%. All were female (Table II).

Table II : Description of clefts according to phenotype and sex.

Classification		M	F	Total (%)
Primary Cleft Palate	FL	12	18	30 (39,5)
	FL+FA	4	8	12 (15,8)
	Total	**16**	**26**	**42 (55,3)**
Secondary Cleft Palate	FVP	0	2	2 (2,6)
	FPO	0	2	2 (2,6)
	Total	**0**	**4**	**4 (5,2)**
Primary and Secondary Cleft Palate	FL+FA+FPO	0	2	2 (2,6)
	FL+FA+FPO+FVP	10	18	28 (36,9)
	Total	**10**	**20**	**30 (39,5)**

Cleft lip (FL) ; Cleft alveolar (FA) ; Cleft Palate of bone (FPO) ; Cleft Palate (FVP)

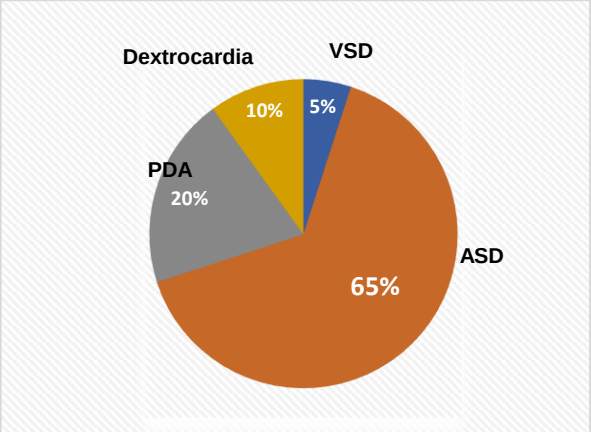
In bi-variate analysis, there was an association between alcohol consumption during pregnancy (p<0.001), fever in the first trimester (p=0.006) and the type of cleft lip and palate observed. There was no association between smoking and the type of cleft observed (Table III).

Table III : Association between pregnancy history and cleft type.

	Primary CP Total=42 N (%)	Secondary Total =4 N (%)	Primary and secondary CP Total =30	P value
Alcohol in pregnancy				**0,001**
Yes	4 (9,5)	4 (100)	6 (20)	
No	38 (90)	0 (0)	24 (80)	
Tobacco in pregnancy				0,2
Yes	0 (0)	0 (0)	2 (6,7)	
No	42 (100)	4 (100)	28 (93,3)	
T1 fever				**0,006**
Yes	6 (14)	2 (50)	0 (0,0)	
No	36 (86)	2 (50)	30 (100)	

CP: cleft palate . T1 = first trimester in pregnancy

In our series, 26.3% of patients had a congenital heart defect, 60% of whom were girls. The most common anomaly was CIA with a proportion of 17.1%. Left-right shunts accounted for 90% of cardiac defects, while positional anomalies had a frequency of 10%.
Figure 1



VSD = Ventricular Septal Defect ;
ASD = Atrial Septal Defect ;
PDA = Patent Ductus Arteriosus
Figure 1 : distribution of cardiac anomalies.

A heart murmur was noted on auscultation in 4% of patients. Holt-Oram syndrome was identified in 5.2% of patients. The evaluation of the systolic and diastolic functions of the heart was normal in all our patients.
Statistically significant associations were found, however, for the variables unexplained death (p = 0.004); heart murmur (p = 0.02); and ancillary malformations (p = 0.03) with the presence of a cardiac anomaly. There was no association between sex and the presence of a congenital heart defect (p = 0.5).
Cardiac anomalies were equally distributed between primary and secondary cleft palate carriers. No cardiac abnormalities were found in secondary cleft palate carriers (table IV). Cleft type did not determine the type of cardiac defect (P-value = 0.69).

Table IIV : Association between type of cleft lip and type of heart defect.

	Type of malformation						
Type of CP	**VSD**	**ASD**	**PDA**	**DC**	**Normal**	**df**	**P**
Primary CP	1	5	2	2	32	8	0,69
Secondary CP	0	0	0	0	4		
Primary and secondary CP	0	8	2	0	20		

CP : cleft palate. VSD = Ventricular Septal Defect ; ASD = Atrial Septal Defect ; PDA = Patent Ductus Arteriosus. DC : Dextrocardia

DISCUSSION

In this study, the median age was 3 months with an interquartile range of [2-6] months. Our result diverges with those of Pereira et al and Hüseyin et al, who found a mean age of 15 years and 8 days, respectively. This difference could be explained by the fact that in the study of Pereira A et al, patients of all ages were included, whereas in Hüseyin A et al, the study population was exclusively composed of newborns [3,4].We found a female predominance in our series with a sex ratio M/F of 0.52. Our result is similar to that of Olufemi et al in Nigeria in 2021 who found a predominance of females, with a sex ratio M/F of 0.82 [5].
Toxicological antecedents in pregnancy, in particular tobacco and alcohol consumption, were recorded in 2.7% and 18.4% of patients in our study. These results are largely below those found by Ting Sun et al in China in 2013, where the proportions of these histories were respectively for alcohol and tobacco; 23% and 38.6% [2]. This could be explained by the difference in culture in our two study regions, with women consuming less tobacco in our setting.
A heart murmur was found in 4% of the patients and all of them had a congenital heart defect. Musculoskeletal anomalies were found in 5.2% of patients and renal anomalies in 2.7% of patients. In the literature, the most common associated anomalies found in cleft lip and palate patients are facial and musculoskeletal; cardiovascular anomalies are excluded [4,6,7].
Primary cleft palate dominated the picture, with a percentage of 55.3%.Our data are similar to those of Akhiwu I et al in Nigeria in 2017 who found a higher frequency of primary cleft palate of about 61.2% [8]. However, they were different from those of Ting Sun et al, who found a predominance of primary and secondary palate clefts at 65.5% [2]. This difference could be attributed to race.
Alcohol consumption during pregnancy was associated with the occurrence of cleft palate (p < 0.001) in our study, as was hyperthermia in the first trimester of pregnancy (p= 0.006). Ting Sun et al found an association between a

history of alcoholism in pregnancy, smoking in pregnancy, fever in the first trimester of pregnancy due to Influenzae and the presence of a cleft lip and palate [2].

Our study also shows that cleft lip and palate was more frequent in girls than in boys. A result that contrasted with that of Ahkiwu I et al [8]. This could be explained by the distribution of our population which was predominantly female.

In our series, 26.3% of the patients had a cardiac anomaly. Our result was close to those of Barrett W et al and Olufemi A et al who respectively found prevalences of about 25.8% and 30.7% [5,9]. But was below the values found by Pradubwong S et al in Thailand in 2014 and Ting Sun et al in China, respectively 41% and 45.1% [2,10]. This difference could be explained by the greater exposure of women in Asia to the toxicants involved in malformative processes.

The majority of the carriers of congenital cardiac anomalies were female (60%). This result is consistent with that of Olufemi A et al, who found that 52.2% of the cases were female [5].

AIC was the most common cardiac anomaly at 17.1%. This result is in agreement with Barret W et al who found a predominance of ASD in the order of 23% [9]. Olufemi A et al found a predominance of IVC. No cyanogenic cardiac anomaly was found.

In our study, we found 5.3% (n=4) with a syndrome. Holt-Oram syndrome was the only one found. Our result contrasts with those of Priyadharshini R et al in 2017 in Thailand or Ting S et al in China who found at least 3 syndromes of which the most frequent were microdeletion 22q11, and velocardiofacial syndrome [2,11]. The high percentage of consanguineous marriage in their study regions and the underdiagnosis of genetic syndromes associated with congenital cardiac anomalies in our environment could explain this situation.

In our study, there were no associations between cleft groups and the presence of a heart defect (P=0.69). This result is similar to that of Olufemi A et al in Nigeria in 2021 [5].

The main limitation of this study was its retrospective nature, making data collection and completion difficult.

CONCLUSION

The prevalence of congenital cardiac anomalies is high in children with cleft lip and palate. Cardiac ultrasound is essential for their cardiac evaluation for facial reconstructive surgery, as these anomalies may go unnoticed clinically and increase perioperative mortality.

DECLARATIONS

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