Objective. The purpose of this study was to investigate the distribution of different cleft patterns by sex, side of the cleft, and family history of clefts in a referral hospital in the south of Spain.

Study design. One hundred twenty-three consecutive cleft lip subjects, with or without palates, attending the Stomatology Unit in the Virgen del Rocío University Hospital and in the Virgen Macarena University Hospital from October 2009 to May 2010 were studied.

Results. The unilateral complete cleft lip and palate (54.4%) was most frequently found, followed by the bilateral complete cleft lip and palate (16.3%). Male patients (60.97%) and the left side (41.46%) were the most affected. A positive family history was observed in 21.94% of subjects.

Conclusions. The most frequent profile in the affected population was male with left unilateral complete cleft lip and palate. The high incidence of family history of cleft on the father’s side prompts us to recommend further genetic research in this area. (Oral Surg Oral Med Oral Pathol Oral Radiol 2012;114(suppl 5):S1-S4)

Cleft lip and palate (CLP) are among the most frequent congenital anomalies of the head and neck. Individuals affected by this kind of anomaly require treatment from a multidisciplinary team from the moment of birth well into adulthood. The functional, esthetic, and social consequences that it entails have a direct impact on subjects and families alike regarding psychologic problems and reduced quality of life.1,2

In general terms, the incidence is estimated to be between 0.8 and 1.7 cases per 1,000 live births.3-6 According to the literature, the incidence of clefts may be influenced by geographic, racial, and socioeconomic factors.7 Murray et al.8 reported an incidence of 1.94 clefts per 1,000 births in the Philippines. In Japan, the incidence was 2.13 clefts per 1,000 births.4 In Brazil, a study conducted by Martelli-Júnior et al.9 recorded a rate of 1.46 cleft cases per 1,000 live births. In Europe, significant differences in prevalence were found between registries and within countries.10 The incidence in Spain ranged between 0.5 and 1.44 clefts per 1,000 live births.11,12

Regarding the frequency of the side affected, one study in Mexico13 found that a cleft lip, with or without palate, tends to occur on the left side and in male patients; likewise, in Kenya,14 male patients predominated and most were left-sided clefts. In Europe,10 a tendency toward a prevalence of females was observed (sex ratio 0.78), particularly among isolated cases (that is, with no other multiple congenital anomalies).

The variations in prevalence of CLP between countries and ethnic or racial groups that different researchers have found5,15,16 need to be further defined for a better understanding of CLP etiology; this was the summary of the “Prioritizing a Research Agenda for Orofacial Clefts” workshop17 conducted by the National Center of Birth Defects and Developmental Disabilities at the Centers for Disease Control and Prevention. The purpose of the present study was to determine the epidemiology and pattern of CLP patients presenting at the Stomatology Section of Virgen Macarena University Hospital (VMUH) referred to Virgen del Rocío University Hospital (VRUH), Seville, two hospital serving southern Spain. There have been no similar studies carried out in Spain with this purpose or characteristics.

MATERIALS AND METHODS

The study included 127 consecutive cleft patients with no recognized associated syndromes, who were seen at the VMUH between October 2009 and May 2010.
Altough Spain lacks to any reference hospital, The VRUH and VMUH, where the study was conducted, are national teaching hospital in Seville, Spain, which treat the majority of the cleft patients who live in southern Spain (Andalucía). In 2009, the population of Andalucía formed 17.82% of the total in Spain. All cleft patients in treatment at the Stomatology Section of Virgen Macarena University Hospital (VMUH) referred to Virgen del Rocío University Hospital (VRUH) between October 2009 and May 2010 were able to be included. All files were retrieved from the records department. Before subjects could be included in the study, they had to have full knowledge and provide written consent, in accordance with the ethical principles governing medical research and human subjects, as laid down in the Helsinki Declaration (2002 version, available at: http://www.wma.net/e/policy/b3.htm). The data were treated with absolute confidentiality. Methods of data collection and storage are subject to the Spanish Organic Law governing personal data protection. The Experimental Ethics Committee at the University of Seville independently approved the protocol. Patients who failed to provide consent or whose records were incomplete were excluded from the study.

All subjects were examined by an experienced doctor specializing in treating patients with isolated clefts or clefts associated with multiple anomalies. Epidemiologic data emerging from the histories were recorded, along with those taken from the physical examination of the anatomic structures involved. Socioeconomic status was also queried.

Subjects were grouped as follows: cleft lip and alveolus (CL), which included complete or incomplete preincisive foramen clefts; cleft lip, alveolus, and palate (CLP), which included transforamen and pre- or postforamen clefts; and cleft palate (CP), which included all postforamen clefts. The CL, CLP, and CP types were further subdivided into unilateral and bilateral, and again according to side (left or right). CLP and CP types were also subdivided into complete (hard and soft palate cleft) and incomplete (no hard palate cleft).

The data obtained were analyzed with the use of SPSS 17.0 software for Windows (Lead Technologies). A univariate analysis of the results consisted of a descriptive analysis of the quantitative variables (mean and standard deviation), with a 95% confidence interval. Bivariate analysis was tested using the χ² test. Results were considered to be significant at P < .05.

RESULTS
Of the initial 127 subjects selected, 123 were finally included in the study. Patients were excluded from the study because of incomplete data and/or failing to provide consent. A total of 97.3% of the study subjects were white and their mothers had resided in one of the regions of southern Spain during pregnancy. The remaining 2.7% corresponded to nonwhite immigrants originating from South America. All patients were of low or medium socioeconomic status.

The cleft distribution results for these subjects showed that CLP was found the most frequently (78.04%; Table I) and CL the least (7.31%). The most common cleft type was the unilateral complete cleft lip and palate (UCCLP; 54.4%; Figure 1). The study confirms a greater prevalence of clefts in male (60.97%) over female (39.02%) subjects (Table I); this greater prevalence affects CLP (47.15% of 78.04%) and CL.

<table>
<thead>
<tr>
<th>Table I. Cleft distribution according to sex, n (%)</th>
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<td>Cleft classification*</td>
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*CLP, cleft lip and palate; CL, cleft lip with or without alveolus; CP, cleft palate.
DISCUSSION

Various epidemiologic studies have evaluated the distribution of orofacial clefts. These were carried out in different countries and regions and among different ethnic and racial groups, because it is accepted that different clefts present different epidemiologies and rates owing to social and demographic variables. In fact, the “Prioritizing a Research Agenda for Orofacial Clefts (OFCs)” workshop, conducted by the National Center for Birth Defects and Developmental Disabilities in 2006, identified “Ethnicity and Population Differences in Orofacial Clefts” as a priority topic for further research in the field, because differences in the incidence of OFC across ethnic and racial groups needed to be defined to understand OFC etiology better.

To the best of our knowledge, there are no earlier studies of a similar kind about the Spanish population. There is an interesting and well-conducted longer study by the EUROCAT working group of the epidemiology of the cleft palate, which was carried out in 16 European countries, including Spain, between 1980 and 1996. In that study, prevalence rates—defined as the number of affected cases per live births, stillbirths, and induced abortions divided by the total number of births—were analyzed, as well as their association with other types of anomaly. Prevalence of clefts and their association with congenital malformation in live births was also studied in Spain. However, in neither of these was the cleft pattern distribution (CL, CLP, CP) analyzed by gender, cleft side, and/or history of cleft in other family members; these are variables which are often analyzed in studies carried out in other countries.

Ninety-three percent of the subjects in the present study were whites from southern Spain. All of them were nonsyndromic subjects of low or middle socioeconomic status who attended the Stomatology Section of Virgen Macarena University Hospital (VMUH) referred to Virgen del Rocío University Hospital (VRUH) for orthodontical treatment. Only nonsyndromic patients were used to avoid interference in the results, because cleft lip and palate associated with a syndrome is considered to be a different clinical entity regarding incidence, etiology, and etiopathogeny. The frequency distribution for clefts, in descending order of frequency, was CLP (78.04%), CP (14.63%), and CL (7.31%; Table I). These results coincide with those found among the population of Iran by Jamilian et al. However, in Brazil and Bolivia, the commonest cleft was CL. In Sweden, a similar incidence of CL, CLP, and CP was found. In Denmark, the combined cleft lip and palate was reported as more frequent (39%) than the isolated cleft palate (27%); this is closer to the results in our population and according to demographic variables that influence cleft epidemiologies and rates.

The population that we studied shows a greater tendency to present isolated cleft lip or in association with a cleft palate in male (60.97%) than in female (39.02%) patients, data which coincide with most studies carried out in different populations: Mexico, Kenya, Brazil, and Sweden. Nevertheless, several authors found that isolated CP by sex this trend was reversed in countries such as Slovenia, Kenya, and Pakistan. Our results show that there were no differences in gender distribution for CP. This is reflected in comparable studies in England and Italy.

Several research studies have mentioned that cleft lip with or without palate occurs more frequently on the left side. According to the results of the present study, the left side was found to be more commonly affected (41.46%) than the right side (27.64%; Table II). These data agree with previously published studies in the international literature.

In our study, 21.94% of patients had an associated family history of CLP. The highest incidence of family-related clefting in our population involved patients with CL (56%). This may be important, but with only 9 CL patients in our population study set, it could be a statistical anomaly not necessarily borne out by a longer-term review of subjects with CL. A significant association with a history of CLP in other family members has been reported in earlier studies. A history of cleft lip and palate among family members of 11.4%
was noted by Srivastava and Bang, and Calzolari et al. Wanjeri and Wachira found that 3.5% of patients had an associated family history of this malformation; the lower percentage may be due to the fact that their study of family history was less exhaustive. The higher percentage of clefts in other family members that we found supports the multifactorial and hereditary characteristic of the cleft as inherited chiefly through the father (15.44%; Table III). Calzolari et al. state that the complex model of inheritance and the frequently conflicting results in different populations on the role of genes that constitute risk factors suggest the presence of real biologic differences. The epidemiologic evaluation can guide genetic research to specify the role of etiologic factors in each different population. For this purpose, it would be necessary in future studies to integrate genetic analysis into epidemiologic studies.

CONCLUSION

We conclude that the unilateral complete cleft lip and palate is the pattern most frequently found in the population of southern Spain. The left side and male sex occur more than their opposites. An associated history of family clefting seems to occur more often on the father’s side of the family rather than on the mother’s. The data indicate that genetic research integrated with epidemiologic studies is necessary to establish a genetic predisposition of cleft lip with or without the palate. Longer-term studies with more subjects are required to evaluate these differences.

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