مستشفى الملك فيصل التخصصي ومركز الأبحاث
King Faisal Specialist Hospital & Research Centre
Gen. Org. مؤسسة عامة
مركز الأبحاث
Research Centre

Cleft Lip / Palate and Craniofacial Anomalies Registry

Cumulative Report
1999 – 2022

Registries Core Facility

Acknowledgments

The Cleft Lip/Palate and Craniofacial Anomalies Registry Committee thanks Dr. Edward Cupler, Executive Director of the Research Centre for his support on the provision of resources for this registry.

We thank all members who had been a part of this registry for their support and dedication, the registry has successfully completed 23 years.

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We also wish to thank all the staff of the Dental, and Plastic Surgery Clinics who provided their valuable assistance to the registrar in facilitating her work at those clinics, and special thanks to all the member of cleft lip & palate \ craniofacial team for their support and dedication in patient ‘s care.

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Message from Principal Investigator

It is with great pleasure to present the Cumulative Report 1999 – 2022 of the Cleft Lip and Palate/ Craniofacial (CLP/CF) Registry.

Twenty-three years ago, it was our dream to build a cleft database, which will provide an accurate resource for researchers, policy makers and other interested health care providers.

It has been an exciting 23 years and we are proud to see the growth of the registry's capacity with time. The functionalities have reached its optimal with more than 2895 patients registered.

Acknowledging the fact that craniofacial deformity is a huge burden on the healthcare system, we thrive to find innovation and techniques to lighten the burden and improve the quality of life for these affected children. However, it is an ongoing effort and hard work to push our goal beyond expectation.

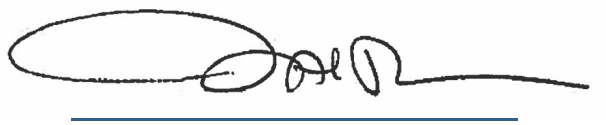
Our main goal is to promote a better understanding of Cleft Lip/Palate and Craniofacial anomalies and to improve the level of care to those affected by it.

I would like to acknowledge the dedication of the cleft and craniofacial team over the years, who strive to provide the best possible long-term health care for the cleft and craniofacial patients.

In addition, I would like to thank all the people who work behind the scenes to make this mission possible. It is our dream that one day stem cell therapy becomes the treatment of choice for the correction of craniofacial deformities, because it will reduce the number of surgical interventions needed for each child, leading to an improvement in the facial appearance and maximizing the child's quality of life. Soon the data will be available online through a infogate page for researchers and interested parties.

My sincere thanks to the Research Centre staff and the staff of biostatistics department for their endless support to keep the registry running.

A Special thanks to the registry data Manager Miss Ebtisam Aljarba for her hard work, and to both Miss Samia Abu Al Hashim and Miss Manal Amarzougi for their support.



Aziza Al Johar,BDS,MsC
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Anomalies Registry

Executive Summary

The Cleft Lip/Palate and Craniofacial Anomalies Registry at King Faisal Specialist Hospital & Research Center (KFSH&RC) is a coordinated collaboration between Department of Dentistry and Department of Biostatistics, Epidemiology and Scientific Computing. Though the registry commenced registering the patients since June 1999. It registered all the cleft lip with or without cleft palate (CLP) patients seen at KFSH&RC irrespective of date of reporting or date of admission to this hospital. However, in case of craniofacial anomalies (CFA), the registration is confined to the patients reporting to KFSH&RC since January 2002. This report is based on the patients registered during the last two years, (1999-2022) a total of 2895 cases were registered. There are 1580 males, and 1315 females, with a male to female ratio of 1.2: 1. Riyadh region has more number of cases (810; 28.2%) , followed by Eastern region (417;14.50%)then Asir region (373;13.0%),

A total of 181 (M=97; F=84) cases were born at KFSH&RC, and the remaining 2714 (M=1483; F=1231) were referred to KFSH&RC from other hospitals. Out of the 2895 patients registered so far, (1963; 67.8%) patients have only CLP, (447; 15.4%) patients have only CFA and (485; 16.8 %) patients have both CLP and CFA. Overall, unilateral cleft lip and palate is (573; 19.8%), and closely followed by bilateral cleft lip and palate (538; 18.6%), however, cleft palate (881;30.4%) is the most common deformity among CLP patients. Out of the 881 total cleft palate patients, there are 394 male and 487 female patients; the female to male ratio is (1.2: 1).

More than half of the patients (1685; 58.2%) parents are consanguineously married and family history of orofacial/craniofacial deformities is reported by (950; 32.8%) patients. Among consanguineously married (602) have familial history, whereas among not related only (344) have family history of anomalies. Out of the (950) patients reported having a positive family history, (521) are males and (429) are females.

The treatment is a long-term process and start soon after birth and can continue well into the second decade of life with a multiple surgeries and long-term speech, orthodontics, ENT/audiological and medical/dental care. The Cleft Lip/Palate and Craniofacial Anomalies Registry was started with a mission “to promote better understanding of Cleft Lip/Palate and Craniofacial Anomalies and to improve patient care and health care in the kingdom of Saudi Arabia.

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List of Tables & Figures:

Introduction:

For all practical purposes, the following definitions/acronyms were used throughout this report.

CL: Cleft Lip, Lip and alveolar cleft

CP: Cleft Palate

CLP: Cleft Lip with cleft palate (both unilateral and bilateral)

CL/P: cleft lip with or without cleft palate

CFA: Craniofacial Anomalies

These twenty three-year reports, based on the patients registered during the period 1999-2022, consists of four sections and can be outlined as below:

Section 1: Background and Registry Functions

This section provides incidence of orofacial cleft and craniofacial anomalies around the world as well as history of this registry. Also describes case definition, patient ascertainment procedures, functionality of the registry including data collection methods, accuracy of the data, software program used, privacy and confidentiality issues of the registry. Subjects and methodology used for this report were also described.

Section 2: Diagnosis and Demographics

In this section the distribution of patients by nationality, region, parental consanguinity, family history and referral hospitals were given by gender and/or major classification of diagnosis. The information's were presented as tables, pie or bar charts.

Section 3: Treatment

This section provides details on treatment such as type of treatment procedures, number of procedures, and place of primary surgeries done etc. by gender.

Section 4: References and Appendices

This section consists of copy of data acquisition forms, data request form, data request policies and procedures. Also includes references and list of publications.

Section 1:
Background and Registry Functions:

Orofacial clefts (OFCs) are considered one of the most common birth defects in all populations of the world. The formation of such is a complex multi-factor in origin. Though various genes and environmental factors are thought to play an important role in its etiopathogenesis, [1],but the cause of this abnormalities still remains poorly understood. Orofacial can be classified into syndromic and non-syndromic, the syndromic rate of such is (30%) while non-syndromic rate is (70%) Non-syndromic occur in isolation without other abnormalities Non-syndromic includes 3 subgroups: cleft lip (CL), cleft palate (CP), and cleft lip and palate (CLP). As to the prevalence, the rates vary based on ethnicity and geography of the countries, and according to most recent data taken from 55 countries, the highest incidence rates of CLP were reported in Venezuela 38 cases/10,000 births, then Iran with rate of 36 cases/10,000 births and finally Japan with rate of 30 cases/10,000 births [2]and in the US , CL with or without CP is the second most common birth defect, affecting one in every 940 births[3] Furthermore, both the CLP and CP rate are higher among Far East Asians and Pacific Islanders than among whites, with the difference being significant for Far East Asians with CLP rate and for Pacific Islanders with CP rate. While the CLP rate is significantly higher among Filipinos than among whites, and the CP rate is lower than whites. The prevalence of CP does not vary in different racial backgrounds, whereas the prevalence of CLP varies considerably, with Asian and American Indians having the highest rate and Africans the lowest, Forrester and Merz [4] ,The birth prevalence in Saudi Arabia for CLP was comparable to global figures, the CL:CLP ratio was high, and only CP was significantly associated with consanguinity Sabbagh, Innes [5]. In a study channeled through the Human Genetics Program of the World Health Organization describing the Prevalence of Cleft Lip With or Without Cleft Palate, shows that the registries in Japan, Mexico-South America, Western Europe, and Canada had a statistically higher prevalence than the overall estimate (9.92 per 10,000 births); whereas, the registries in Eastern Europe, South-Mediterranean Europe, and South Africa had a statistically lower prevalence[6].

Given the public health importance of birth defects, it is necessary for birth-defect surveillance systems to monitor and detect trends in birth defects, provide data for etiologic studies of birth defects, and provide the basis to plan and evaluate the effects of prevention activities Mossey and Catilla [7]. These purposes are best accomplished through surveillance systems that use multiple data sources, possess accurate and precise diagnostic criteria, perform timely data analysis, dissemination of the data, and use personal identifiers for follow-up and data linkage.

King Faisal Specialist Hospital and Research Centre (KFSH&RC) established the Cleft Lip/Palate Registry by mid-1999 and started collecting data on CLP patients attending to KFSH&RC. Later in 2002, this registry changed its name to “Cleft Lip/Palate and Craniofacial Anomalies Registry” with the inclusion of Craniofacial Anomalies in its scope. This registry is a coordinated collaboration between the

Department of Dentistry and Department of Biostatistics, Epidemiology and Scientific Computing (BESC)

Functionalities of the Registry

Case Definition:

The congenital malformations associated with the craniofacial anomalies cover a wide range of birth defects. The fact that orofacial clefts are easily described in the newborn, as compared to some other congenital birth defects, makes their inclusion into the registry easy and complete. However, the different types of clefts as well as the variety of conditions in which orofacial clefts occur require careful classification as to whether the individual to be included or not. The criteria for patient registration in the registry are defined as below:

A person who is diagnosed as having.

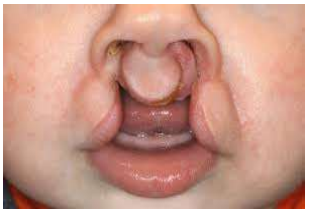
Typical orofacial cleft (cleft lip, cleft palate, cleft lip and palate) * or

Other types of facial clefts – ear, eye, orbit deformities)

Craniofacial anomalies**

The eligibility of the case did not change based on whether the cleft is complete or incomplete. unilateral or bilateral; isolated or associated with another anomaly.

* Cleft lip is defined as “congenital failure of the maxillary and median nasal process to fuse, forming a groove or fissure in the lip”.



Bilateral CLP

Unilateral CLP

*Cleft palate is defined as “congenital fissure in the roof of the mouth, resulting from incomplete fusion of the palate during embryonic development. It may involve only the uvula or extend through the entire palate”.

** The term “craniofacial deformities” literally encompasses all deformities of the cranium and the face. More specifically the term has come to imply those congenital anomalies of the head that interfere with physical and mental wellbeing.

Case Ascertainment:

The registry collects data from multiple sources to create a comprehensive listing of patients diagnosed with orofacial /craniofacial anomalies. Data sources includes.

1. Medical record of the patient
2. Interviewing patient and their family.
3. Power chart
4. Care Stream R4, Dental system

There are two CLP clinics per month. One clinic for new patients, while the second clinic for follow-up patients.

Patients are also referred to another clinic as needed.

Other areas from where CLP patients can be ascertained are:

- Plastic Surgery Clinic
- Surgery, Urgent Add-On Clinic
- Neurosurgery Clinic
- Craniofacial surgery
- Orthognathic surgery
- CLP Combined clinics.

Data Set:

Data is collected on a two-part register form (Appendix I) approved by the Registry Committee. The registrar is responsible for the data collection, data entry and validation.

The details collected for the registry includes the basic demographic variables (age, sex, area of residence etc.), diagnosis detail (lip or palate, unilateral or bilateral, craniosynostosis: syndromic, or non-syndromic etc.) and procedures (lip adhesion, alveolar bone graft, Pharyngeal flap, craniofacial surgery, speech therapy etc.). The medical diagnoses were coded using the LAHSHAL System of nomenclature [Kriens 1989] in parallel to the International Classification of Diseases Clinical Manifestation 10th edition (ICD-9CM).

Activities of the Registry

Data Acquisition:

Data are collected in two phases using structured questionnaire. The first phase takes place when the patient encounters the clinic for the first time. After confirming that the patient satisfies all the

inclusion criteria of the registry, preliminary data on diagnosis and patient's demographic data are collected by face-to-face interview. It was then assigned a unique registration number of eight digits, consisting of year of registration (4 digits) and serial number in that year (4 digits).

The second phase involves uploading facial photographs, and radiographs that are taken through CS R4 dental clinic system and collecting further information about the registered patients. These data include clinical diagnosis and treatment, which are coded using ICD 9 CM and local codes. The collected data were then entered in the registry database through in house developed software. Periodical verification of the data set was taken place and documented. Lapse in the registration process, if any, will be identified and suitable recommendations for enhancing performance and accuracy of data entry method/personnel will also be discussed and implemented.

Software Design:

The software used for data entry and analysis is a web based online registration system with SQL 2005 database as a back end and internet-enable design as a front end. The Web Server used for the design of the Cleft Lip/Palate & Craniofacial Anomalies Registry is the Microsoft Internet Information Server (IIS). The database structure is developed with Platinum Erwin version 3.5.2 for entity relationship modeling. The database including all the tables, indexes, rules, stored procedures, views, and triggers is created and maintained with Microsoft SQL Server 2005.

Only authorized users with various levels of security can access the registry software over the web. Some additional security checks like cookie setup and time-out feature are incorporated within the registry as secondary measures of security.

In addition to several security checks, the system is designed as such that there are three major kind of users that can have access to the registry software with defined set of privileges:

These users can be categorized as:

Admin users: with administrative rights like creating new users, data validation, data deletion and modifying static table information in addition to full control on data entry and update modules.

Common users: with limited data entry and data modification privileges.

Browse only users: no deletion, export privileges and without any data modification.

Validation:

All the data entry forms have validation checks and warning messages that restrict users from making any data entry mistakes. Validation rules were designed as a quality check for the data entered in the registry. The diagnosis validation rules that were integrated and are run routinely to confirm accuracy of coding.

Privacy and Confidentiality Issues:

Technologies now allow personally identifiable health information to be easily collected, correlated and widely transmitted, renewing concerns over privacy and confidentiality. It is generally accepted that information provided by patients to the health service is provided in confidence and must be treated as such so long as it remains capable of identifying the individual it relates to. Since the registry is collecting personally identifiable health data, one of the major responsibilities of the registrar is to ensure privacy as a fundamental consideration in collection and maintenance of the information obtained. It is also realized by the registry staff that mistakes in handling or protecting health data might result in revealing the intimate details of innocent people's lives. The Registries Core Facility section under BESC department ensures that only authorized individuals should handle the raw data as well as the registry database and is accessible to the right people through assigned passwords. Registry data will be released to the researcher after proper approval from the registry committee, which makes sure that privacy of individual's does not supersede other rights or societal goals while carrying out the research. Data request form, data request policies and procedures are available in the Appendices.

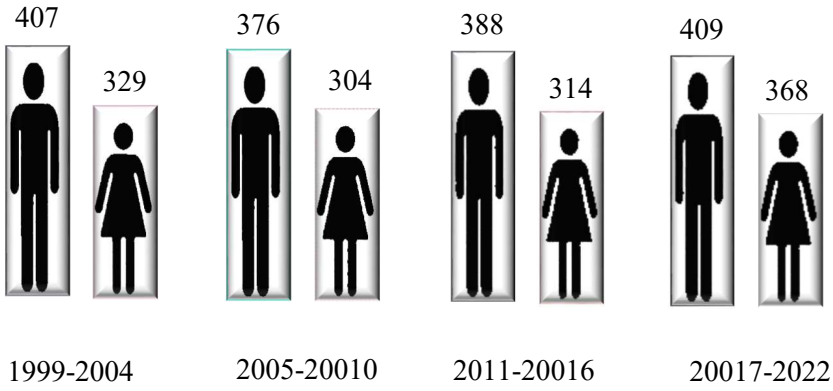
Subjects and Methods:

This report is based on all the patients registered since 1999 until December 2022. Descriptive statistics such as frequencies and percentages were obtained using SAS software (for Windows, version 9.3). This information was presented as tables, pie or bar charts as applicable.

Section 2: Diagnosis and Demographics

Over the twenty-three years period (1999-2022) this registry registered a total of 2895 patients (M= 1580; F= 1315). The distribution of patients over the years by gender is shown in Figure 2.1. It is worth to remember that the registration of craniofacial anomalies by the registry was taken since January 2002 .

Figure 2.1: Distribution of Cases by Year of Registration at KFSH&RC



Distribution of Anomalies:

Out of the 2895 patients registered so far, 1963 patients had only CLP, 447 patients had only CFA and another 485 patients had both CLP and CFA (Table 2.1).

Table 2.1: Distribution of Cases by Anomalies

Diagnosis	Male	Female	Total	%
CL/P	1092	871	1963	67.8
Craniofacial	230	217	447	15.4
CL/P & CF	258	227	485	16.8
Total	1580	1315	2895	100.0

Distribution of Cleft Lip and Palate:

There were 1350 males and 1098 females with CLP. Cleft palate was most common deformity followed by unilateral CLP and bilateral CLP. Overall, the male to female ratio is 1.23:1. However, a female preponderance was observed among cleft palate; lip / alveolar cleft, and midline cleft (Table 2.2).

Table 2.2: Distribution of Cleft Deformities by Gender

Cleft Deformities	Male	Female	Total
Cleft Lip	140	73	213
Lip and Alveolar Cleft	104	108	212
Cleft Palate	394	487	881
Unilateral Cleft Lip and Palate	354	219	573
Bilateral Cleft Lip and Palate	347	191	538
Midline Cleft	10	19	29
Alveolus and Palate	1	1	2
Total	1350	1098	2448

Distribution of craniofacial anomalies:

Out of the 935 total craniofacial patients there were 490 male and 445 female patients with a male to female ratio of 1.9:1. More than half of the patients (544) had only facial, (326) had only cranial and (65) had both anomalies (Table 2.3)

Table 2.3: Number of Craniofacial Cases by Gender

Cranial / Facial Status	Male	Female	Total
Cranial Only	181	145	326
Syndromic	47	46	93
Non Syndromic	134	99	233
Facial Only	276	268	544
Both (Cranial and Facial)	33	32	65
Syndromic	9	11	20
Non Syndromic	24	21	45
Total	490	445	935

Regional Distribution:

Total of 2868 cases were from Saudi Arabia (Regardless of their nationality). Riyadh region had more number of cases (810 ; 28.2 %) followed by Eastern region (417; 14.5%) and Asir (373 ; 13.%) (Figure 2.2). Arc Info, GIS software is used to create the map showing distribution of the

cases according to the 13 administrative regions of Saudi Arabia. Table 2.4 gives distribution of patients by regions of Saudi Arabia

Figure 2.2: Distribution of the Cases by Regions of Saudi Arabia

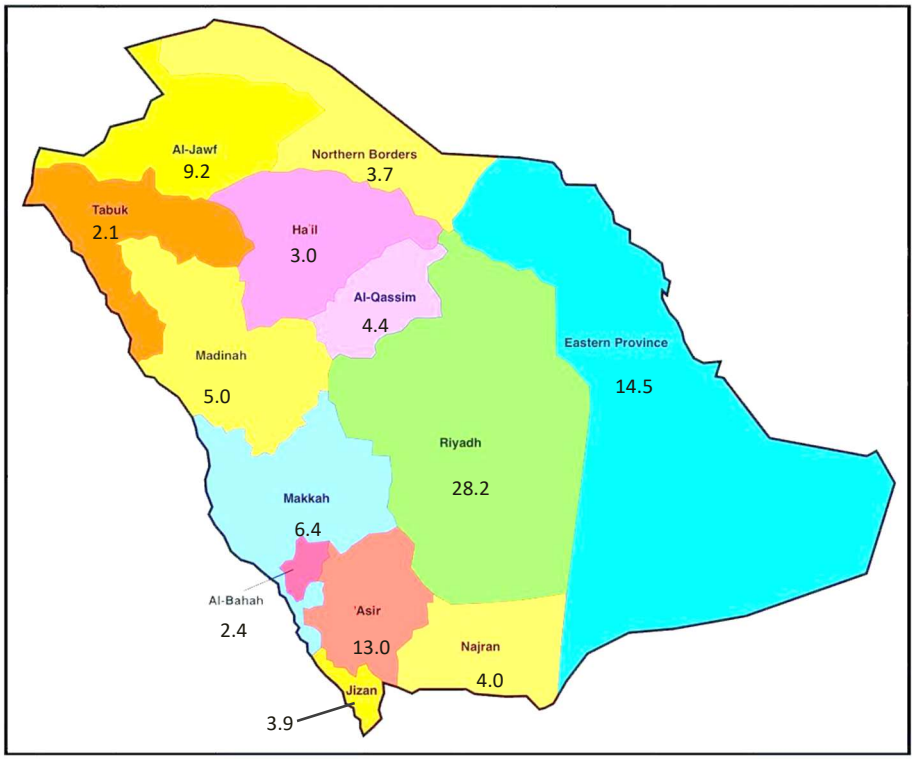


Table 2.4: Distribution of Patients by Regions of Saudi Arabia:

Area of Residence	Male	Female	Total	%
Saudi Arabia	1570	1298	2868	99.1
Riyadh	445	365	810	28.2
Eastern Province	218	199	417	14.5
Asir	214	159	373	13.0
Al Jouf	127	138	265	9.2
Makka	92	92	184	6.4
Madina	91	53	144	5.0
Qasim	81	45	126	4.4
Najran	64	52	116	4.0
Jizan	65	46	111	3.9
Northern Province	57	50	107	3.7
Hail	45	41	86	3.0
Baha	35	34	69	2.4
Tabuk	36	24	60	2.1
Outside Saudi Arabia	10	17	27	0.9
Total	1580	1315	2895	100.0

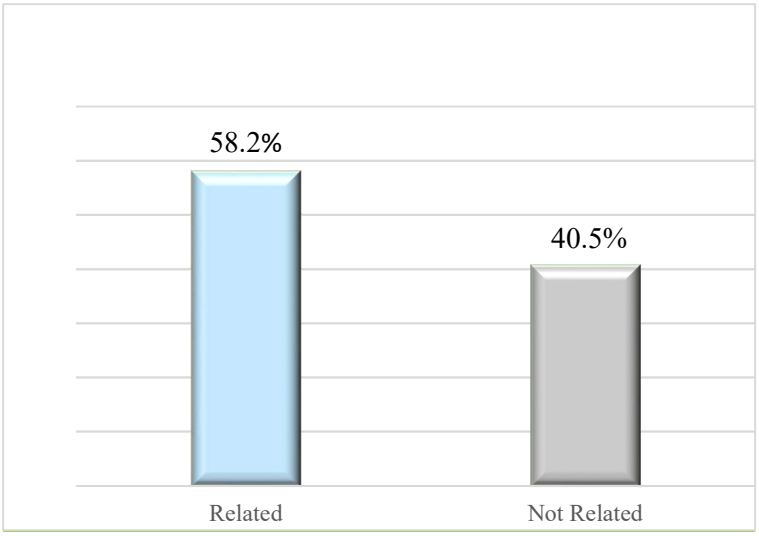
Consanguinity:

More than half of the patients' parents are consanguineously married 58.2% while in 40.5% patients the parents are not consanguineously married. The parental consanguineous status is not known for 38 patients. Table 2.5 shows status of parental consanguinity according to major classification of anomalies.

Table 2.5: Consanguinity by gender

Consanguinity	Male	Female	Total	%
Related	938	747	1685	58.2
Not Related	620	552	1172	40.5
Not Available	22	16	38	1.3
Total	1580	1315	2895	100.0

Figure 2.3: Distribution of cases by consanguinity



Family History:

Family history of orofacial/craniofacial deformities is reported by 950 (32.8 %) patients. Out of the 950 patients reported having a positive family history, 521 are male and 429 are female. Table 2.6 shows status of familial history by major classification of anomalies.

Table 2.6: Family History by Major Classification of Anomalies

Familial History	CL	CP	CLP	CF	Total
Yes	196	259	450	45	950
No	244	617	653	396	1910
Unknown	.	.	2	.	2
Not Asked	8	14	5	6	33
Total	448	890	1110	447	2895

Figure 2.4: Family History Status among Cases

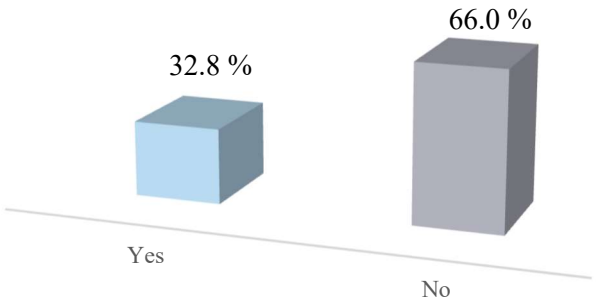


Table 2.7 shows relationship of affected family members to the patient. Among the first degree relatives, siblings had history of deformities more than any other relations. Siblings of 124 male patients and 101 female patients are affected either by orofacial or craniofacial anomalies.

Table 2.7 Relationship to Patient among Positive Family History by Gender

Family History = Yes	Male	Female	Total
Father	12	8	20
Mother	5	7	12
Siblings	124	101	225
Other Relatives	288	242	530
Mother & Siblings	4	4	8
Mother & Other Relatives	5	4	9
Father & Siblings	13	10	23
Father & Other Relatives	9	7	16
Mother, Siblings & Other Relatives	2	.	2
Father, Siblings & Other Relatives	11	5	16
Siblings & Other Relatives	48	41	89
Total	521	429	950

Consanguinity by family history:

Table 2.8 shows the number of patients by their family history of orofacial cleft and parental consanguinity status. Among consanguineously married 58.2% (602/1685) had familial history whereas among not related only 40.5% (344/1172) had family history of anomalies.

Table 2.8: Number of Cases by Consanguinity and Family History

Consanguinity	Family History				Total	
	Yes	No	Unknown	Not Asked	Count	%
Related	602	1071	2	10	1685	58.2
Not Related	344	824	.	4	1172	40.5
Not Available	4	15	.	19	38	1.3
Total	950	1910	2	33	2895	100.0

Referring Center:

Table 2.9 gives distribution of patients according to referring centers by Gender.

Table 2.9: Referring Centers by Gender

Referring Centers	Male	Female	Total
King Faisal Specialist Hospital	97	84	181
Others	1483	1231	2714
Total	1580	1315	2895

Though all the patients mentioned in this report were registered from KFSH&RC, Figure 2.5 highlights the distribution of patients according to origin of the hospital/center. Only 181 (M=97; F=84) patients were born and registered from KFSH&RC, and the remaining patients were referred to KFSH&RC from other hospitals that are scattered all over Saudi Arabia.

Figure 2.5: Referring Centers

Distribution of Cleft Deformities by Other congenital anomalies:

The prevalence of associated anomalies among cleft patients are high. Cardiac anomalies are one of the most common congenital disorders associated with cleft lip / palate patients with its various types, including ventricular septal defect, atrial septal defect, and etc., where out of the 2448 CLP patients,267 (10.9%) patients have cardiac anomalies, see the below table 3.1, then followed by digital anomalies 116 (5%) table 4.9, and the last common defect associated with the orofacial cleft are the genital abnormalities 66 (2.7) table 3.3 . see the below tables:

Table 3.1: CLP & CHD

CLP & CHD	CL	CP	CLP	Total
Male	20	46	68	134
Female	23	60	50	133
Total	43	106	117	267

Table 3.2: CLP & digital anomalies

CLP with digital anomalies	CL	CP	CLP	Total
Male	7	36	19	62
Female	7	37	14	58
Total	14	73	33	120

Table 3.3: CLP & genital anomalies

CLP with genital anomalies	CL	CP	CLP	Total
Male	6	27	21	63
Female		1	2	3
Total	6	28	23	66

Section 3: Treatment:

Clefts are surgically repaired with some functional and cosmetic restoration, but often series of treatments are necessary until the child is of school age or more.

Place of Primary Surgery:

Table 3.4 shows distribution of patients according to the place where the primary surgeries (Initial lip & nose repair, Initial palate repair) were done. Out of the 1499 initial lip repair 1015 (67.7%) were done at KFSH&RC and out of 1785 initial palate repair 1375 (77.0%) were done at KFSH&RC.

Table 3.4: Place of Primary Surgeries

Hospital	Procedure Type						Total	
	Initial Lip Repair		Initial Nose Repair		Initial Palate Repair			
	N	(%)	N	(%)	N	(%)	N	(%)
KFSH&RC	1015	67.7	684	92.2	1375	77.0	3074	76.4
Other	484	32.3	58	7.8	410	23.0	952	23.6
Total	1499	100.0	742	100.0	1785	100.0	4026	100.0

Section 4: References and Appendices

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