

# Prevalence of Cleft Lip and Palate in the Developing Countries of Asia and Africa: A Review

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## Abstract

**Introduction:** The objective of this paper is to review the literature on the incidence of cleft lip and palate (CLP) in the developing countries of Asia and Africa. The existing literature tends to focus on developed countries and there is lack of research in developing countries.

**Methods:** The studies that met the inclusion criteria were reviewed and data extracted. There were 20 studies done in Asian and African countries which were included.

**Results:** The incidence of CLP in Asian countries is markedly greater than in African countries. Most studies report a male predominance in CLPs and a female predominance in cleft palates. The male dominance is seen more than other developing countries which is consistent with other Asian countries and the same has been found in African countries. In the Nepalese study, females were slightly more affected than males among all clefts. The incidence or prevalence in the frequency and types of malformations of CLP in developing countries has been provided.

**Conclusions:** The review underlines the need for an aggressive approach to prevent and control CLP in patients in developing countries.

## Introduction

Cleft lip and palate (CLP) are common malformations of the head and neck and account for approximately 65% of malformations in the head and neck region.<sup>1,2</sup> CLP originates from failure in fusion of the numerous oronasal processes within the first five to six weeks of gestation.<sup>3</sup> CLP involve structures around the oral cavity and in a complete craniofacial deformity include adjacent areas, the lip and the palate.<sup>4</sup> Depending on the elemental characteristics of the embryology, anatomy and physiology of the defect, the varieties of CLP are categorized as: i) involving the lip and alveolus ii) involving the lip and palate iii) involving the palate alone and iv) congenital insufficiency of the palate.<sup>5</sup> Several associated factors have been identified, namely pre-maternal obesity and overweight women,<sup>6,7</sup> parental consanguinity,<sup>8</sup> passive smoking,<sup>9</sup> and certain genetic markers.<sup>10</sup> CLP has also

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been associated with several factors that may affect the expectant mother early in the first trimester of pregnancy. These include infection and toxicity, poor diet, hormonal imbalance, and genetic interference.<sup>5</sup> CLP is a group of heterogeneous birth defects that could result in infant malnutrition, poor speech outcomes, impaired social development, and elevated infant mortality rates.<sup>11</sup>

There is substantial variability of the incidence of CLP related to geographic origin, ethnicity, and socioeconomic conditions.<sup>2</sup> The prevalence is higher among Asians and North Americans followed by Caucasians and lowest among African populations.<sup>2,12,13</sup> A systematic review has shown pooled birth prevalence of undifferentiated CLP as 1.38 per 1000 births (95% CI 1.20-1.56).<sup>14</sup>

There is limited data regarding incidence and prevalence of CLP in developing countries. Among the Asians, the reported rate was 1.33 per 1000 live births, 1.3 for Chinese, 1.34 for Japanese and 1.47 for other Asians.<sup>12</sup> The incidence among Indians was 0.93 per 1000 births for CLP and 0.17 per 100 births for cleft palate (CP).<sup>13</sup> In many African countries' prevalence, estimated from hospital-based data, ranges from 0.2 per 1000 live births in Ethiopia to 1.7 per 1000 reported in Kenya.<sup>15</sup> Likewise, in Nepal the total birth prevalence of CLP was 1.64 per 1000 live births per year.<sup>16</sup> As most of the literature has shown CLP in developed countries, it will be worthwhile to determine the frequency and types of malformations of CLP in developing countries.

The objective of this paper is to review the literature on the incidence of CLP in the developing countries of Asia and Africa. The current existing literature tends to focus on developed countries and there is lack of research in developing countries. A review is therefore required to inform further research in these regions.

## Methods

The search engines used were PubMed, Medline, Scopus, and Google Scholar. The search terms included "cleft lip", "cleft palate", "orofacial cleft", and "epidemiology", "incidence" or "prevalence". Also, comprehensive search terms for developing countries was used e.g. "Developing Countries" or "Developing World" or "Less Developed Countries" or "Low Income Countries" or "Middle Income Countries" or "Middle Income Nations" or "Under Developed Countries" or "Under Developed Nations." All observational studies, consisting of descriptive and analytical, were taken into consideration. Asian and African countries with similar context and resource settings were selected so that they could be part of the study. Studies were included if they reported the birth prevalence of CLP. Systematic reviews and meta-analyses were not considered.

The studies that met the inclusion criteria were reviewed and data extracted. The characteristics recorded were the time of the study, the country, study design, reference population (if any) and the birth prevalence of orofacial cleft. Where available, data for CLP subtypes were extracted. Other variables such as consanguinity, or previous family history of cleft were also included.

The risk of bias was assessed for each individual study based on

the data source, population included in the study, and any special characteristics of the population. Some of the studies included in this review represented data on a wide range of variables, in an inconsistent manner. Data from studies that did not specify if the population included isolated or undifferentiated CLP were classified as undifferentiated and excluded from the analysis.

## Results

The literature search yielded 64 titles which matched the search terms. Of them, 12 were from developed countries and 32 were systematic reviews also from developed countries which were subsequently excluded from the review. Only studies conducted in Asian and African countries were included. Altogether, there were 20 studies which were included in the review.

### CLP in South Asia

In Pakistan, of the 1574 cases of CLP, 1061 (67.4%) were from Punjab, 361 (23%) from Khyber, Pakhtunkhwa, 85 (5%) from Sindh and 67 (4.2%) from Azad Jammu and Kashmir. The number of CLP in males (931) was higher than in females (643).<sup>3</sup> In a study conducted among 80 subjects in Chennai, India, 51 were males and 29 were females. There were 26 study subjects with cleft lip (CL), 28 with CLP and 26 with CP.<sup>5</sup> The incidence and prevalence of cleft lip and / or palate (CL ± P) was 0.1 per 1,000 people and 0.73 per 1,000 people in Gujrat, India.<sup>13</sup> In Nepal, 51 patients with CL ± P were identified among 30,952 live births giving a total prevalence of 1.64 per 1,000 live births per year.<sup>16</sup> Another study showed 418 orofacial clefts in eastern Nepal of which 12 cases which were undifferentiated, hence excluded from the study. Of the total remaining 398 cases, 198 were CL, 103 CLP and 97 CP; females (223) were seen to have more clefts than males (175).<sup>17</sup> Over a 10-month period, the number of babies born with CLP in Patan Hospital, Nepal was 7 (11%).<sup>18</sup>

### Other Asian Countries

In a retrospective study in the Palestinian Territories, during a 10-year period there were 33,239 live births among which 35 cleft lip and /or palate (CL ± P) were seen (1.01/1000 live births) with male dominance of 63% of the newborns.<sup>19</sup> A study in Taiwan showed that there was a decline in the rate of cleft lips with or without cleft palate but a slight increase in the rate of CP. However, the annual rate of incidence of CLP was 1.48 per 1000 live births.<sup>12</sup> The incidence of orofacial cleft in the Philippines was estimated to be 1 in 750 people.<sup>20</sup> A study in Thailand showed a prevalence of 1.57 per 1,000 live births.<sup>21</sup> Another case-control study conducted in 40 hospitals in 6 provinces in Thailand found out that CL ± P were more among males than female infants. The study also revealed that low birth weight (LBW) was statistically significant among cases than in controls.<sup>22</sup> In a case-control study done in Singapore, the prevalence of CLP was 1.72 per 1000 live births.<sup>23</sup> Birth defects in Malaysia showed that CLP was seen in one per 591 live births.<sup>24</sup>

**CLP in African Countries**

Smile Train is a cleft-focused global non-governmental organization (NGO) which provides free corrective surgery for children in 87 countries. It has supported more cleft surgeries than all other global charities combined.<sup>25</sup> The pooled data from seven of the largest Smile Train treatment centres in Nigeria found 2,197 orofacial clefts with a prevalence of 0.5 per 1,000 live births. Over half (53.3%) of the orofacial clefts were in males and 47.7% females.<sup>26</sup> The estimated prevalence of CLP in South Africa was 0.3 per 1,000 live births; with a female prevalence of 52.5% compared to males with 47.5%.<sup>15</sup> An epidemiological study in Tanzania showed a total of 240 orofacial clefts. The most common cleft was isolated cleft lip (CL) constituting 49.2% of all clefts, CLP 39.2% and CP 11.7%. Here too the males (52.9%) were slightly more affected than females (47.1%).<sup>2</sup> In a study

done among cleft patients in Zimbabwe, CLP data from 2006 to 2010 was recorded. Of the 604 patients, 175 represented the CLP group, 106 the CP, and 251 belonged to the CL group. Additionally, males (50%) were seen to predominate females (42%) with the remainder being of unreported gender (8%).<sup>27</sup> The CLP was also seen among the Egyptians, in that among the 1318 patients, 679 were males and 639 were females. The CLP, CL and the CP numbers were 485, 383 and 256 respectively; the remaining 257 had a secondary disease.<sup>28</sup> In a case-control study in Northwest Ethiopia, where 398 newborns were included in the study, 25 of the cases were CLP whereas 75 were other cases.<sup>29</sup> This study also found that there was a positive association with women who took herbal medicine during pregnancy and major structural defects. Alcohol intake during pregnancy was also found to be associated with birth defects.

Table 1. Characteristics and outcome measures from included studies

Reference	Country	Design	Participants	Main findings including prevalence
Sarif et al. (2019)	Pakistan	Retrospective	1574	Male – 931, Females – 643
Nagappan et al. (2015)	India	Descriptive	80	Male – 51, Females – 29; CL – 26, CP – 26, CLP – 28
Khajanchi et al. (2014)	India	Cross-sectional	154	0.73 per 1,000 live births
Singh et al. (2012)	Nepal	Retrospective	51	1.64 per 1,000 live births
Singh et al (2011)	Nepal	Retrospective	398	Male – 175, Female – 223; CL – 198, CP – 97, CLP – 103
Ansari et al. (2014)	Nepal	Cross-sectional	64	CLP – 7
Borno et al. (2014)	Palestine	Retrospective	35	1.05 per 1,000 live births
Chang et al. (2016)	Taiwan	Retrospective	7282	1.48 per 1,000 live births
Muntz et al. (2013)	Philippines	Descriptive		1 in 750 people
Suwantanaviroj et al. (1996)	Thailand	Retrospective	437	1.57 per 1,000 live births
McKinney et al. (2013)	Thailand	Case-control	Case – 86; Control – 172	Male – 49, Female – 37
Thien et al. (1992)	Singapore	Case-control	687	1.72 per 1,000 live births
Thong et al. (2005)	Malaysia	Case-control	253	1:591 per 1,000 live births
Butali et al. (2014)	Nigeria	Descriptive	2197	0.5 per 1,000 live births; Male – 53.3%, Female – 47.7%
Hlongwa et al. (2019)	South Africa	Descriptive	699	0.3 per 1,000 live births; Male – 47.5, Female – 52.5%
Manyama et al. (2011)	Tanzania	Retrospective	240	Male – 127, Female – 113; CL-49.2%, CP-39.2%, CLP-11.7%
Tollefson et al. (2014)	Zimbabwe	Cross-sectional	604	Male - 50%, Female - 42%; U - 8%; CL – 251, CP – 106, CLP – 175
Tsehay et al. (2019)	Ethiopia	Case-control	398	Male – 219, Female – 179; CLP – 25
Abulezz et al. (2017)	Egypt	Retrospective	1318	Male – 679, Female – 639; CL – 383, CP – 256, CLP – 485

## Discussion

This study was conducted to provide information regarding the incidence or prevalence of CL ± P in developing countries. A number of factors are known to affect the prevalence of orofacial clefts, including genetic factors such as ethnicity and family history of clefting as well as environmental factors such as maternal smoking and in utero exposure to seizure medications.<sup>14</sup> The incidence of CLP in Asian countries is markedly more as compared to the African countries.<sup>19</sup> The opportunity to provide free surgical care for orofacial clefts has helped open new avenues for research and treatment outcomes in many Asian and African countries.

A high ratio of consanguineous marriages, lack of formal prenatal counselling, monthly examinations, regular laboratory testing during pregnancy, maternal malnutrition and low use of supplements are thought to be some of the causative factors associated with high ratio of CLP in Pakistan.<sup>3</sup> The association of maternal education and marital status with congenital malformations may reflect the inadequacy of the socioeconomic status and psychological support for pregnant women. Histories of similar anomalies are risk factors in the family for the congenital malformations.<sup>21</sup> Although several epidemiological reviews of CLP have been published, a review of the studies shows that there is no particular trend in different parts of the world. A WHO study published a document to detail the incidence in 13 countries and the incidence varied from 0.22 to 1.64 per 1,000 live births.<sup>16</sup>

Studies conducted in a multiplicity of settings around the world have shown a significant association between maternal fever and birth defects.<sup>29</sup> This was consistent with the study where mothers who had a history of fever during pregnancy were around three times more likely to have babies with birth defects even after adjusting for other factors.<sup>29</sup> Moderate to high levels of alcohol intake during early pregnancy may also result in changes in growth and morphogenesis of foetus.<sup>29</sup>

Most studies report a male predominance in CLP and a female predominance in cleft palate. The male dominance is seen more than other developing countries which is consistent with other Asian countries such as India, the Philippines, and Taiwan. The same has been found in African countries like Tanzania, Zimbabwe, South Africa, and Egypt. However, in the Nepalese study, females were slightly more affected than males among all clefts. This is in contrast to all other studies and also to the data on Caucasian populations.<sup>17</sup>

The financial impact on the family of a person with an unrepaired cleft is not just money oriented. Understanding the financial impact could assist governments of low and middle income countries to strongly consider developing infrastructure for surgical care of the clefts.<sup>20</sup> Programs such as the Smile Train runs in various developing countries taking care of the patients with CLP. Assuming a steady birth rate of new cases, the average age presentation would decrease with each subsequent year. The older children would already have been treated and the program would be aiming at the treatment of those with unmet needs.<sup>27</sup>

This study did not comprise of data from developing countries outside of Asia and Africa. Hence, the conclusions derived are only valid in the countries taken in this study. This review of the literature also accounted for those studies which were not part of systematic reviews and meta-analyses.

## Conclusions

CLP is one of the most common orofacial defects. Children with CLP are subject to unavoidable distress throughout their childhood and into their adulthood. The incidence or prevalence in the frequency and types of malformations of CLP in developing countries has been provided. The review underlines the need for an aggressive approach to prevent and control CLP in patients in developing countries.

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