Burden of Orofacial Clefting in India, 2016: A Global Burden of Disease Approach

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Abstract

Background: In the recent past, there have been inconsistent reports of India witnessing a decreasing trend in the incidence of orofacial clefts (OFC). To date, little comprehensive evidence has been published. To identify the prevalence, associated burden in terms of epidemiological parameters and to estimate the "unmet" OFC treatment needs, the present study was undertaken. **Materials and Methods:** Using the Global Burden of Diseases 2016 approach and its assumptions, an attempt was made to estimate the prevalence to quantify the burden of OFC in India as disability-adjusted life years (DALYs), years of life lost (YLL), and years lived with disability (YLD) as well as death due to OFC. The results from such an approach are presented. Using previous estimates of "unmet" OFC treatment needs, an attempt was made to estimate the current volume of "unmet" OFC treatment needs. **Results:** In the present study, it was estimated that a total of 0.033% of all Indian population suffers from OFC. In 2016, the estimated prevalence rate/100,000 was 33.27 for males, 31.01 for females, and 32.18 combined for both genders. It was estimated that for all ages, the DALYs lost were 2.05 for 100,000 males, 2.66 for females and 2.34 for both sexes. The OFC birth prevalence model revealed that the birth prevalence (as a proportion) in 2016 in India showed an odds ratio of 0.48 (1.56–1.65) and fixed factor of nonrecording 0.83 (0.15–6.63), underreporting 0.97 (0.88–1), gender 1.09 (1.02–1.16), chromosomal diagnoses included 1.22 (1.22–1.22), and stillbirth 1.22 (1.22–1.22). The total unmet cleft treatment need was estimated at 79,430 or 18.76% of the total Indian cleft population with OFC. **Conclusions:** Within the constraints of the mathematical modeling and based on all available surveys, literature, and reported data, the overall birth prevalence and the prevalence of OFC in India are presented. Till reliable data emerges, the present estimates could serve as a robust estimate of the prevalence and burden of OFC in India. The present enterprise highlights the need for well-designed, high-quality Pan-India, community-based, observational studies to accurately estimate the burden of OFC in India.

Keywords: Cleft lip, cleft palate, global burden of diseases, India, orofacial clefts

Introduction

Orofacial clefting (OFC) is one the most common birth defects, causing significant costs in terms of rehabilitation, emotional difficulties, and economics.[1] The condition is considered to be multifactorial and polygenic in nature.[2,3] It is documented that the birth prevalence of children with OFC significantly differs between geographical boundaries.[2,3] However, owing to deficiencies in proper births and birth defect surveillance system in certain geographical parts of the developing world, the prevalence of OFC often is understated.[1,4-6]

India is one of the most populous countries and has a significant prevalence of OFC.[4] The prevalence of OFC in India is being monitored by the Indian Birth Defects Registry[7] and several other databases such as that of the Indian Ministry of Statistics and Programme Implementation, India National Sample Survey,[8] and the survey conducted by the International Institute for Population Sciences (India) in collaboration with the World Health Organization.[9] Peer-reviewed and published literature are often locoregional in nature and originate from isolated parts of India.[10-12]

The burden of OFC in India, measured in terms of disability-adjusted life years (DALYs) and other epidemiological parameter studies are very limited.[13] The Global Burden of Diseases (GBD 2016) is an attempt to mathematically estimate the epidemiological burden of diseases harnessing the power of

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latest disease modeling software programs. The approach relies on data emanating from all available published peer-reviewed literature meeting predetermined standards and collating them using mathematical modeling.[14] The aim of this manuscript is to concisely present the estimated burden of OFC in India in terms of epidemiological parameters in 2016 using the GBD approach.

Materials and Methods

Data input

The data for this study were collected using the GBD 2016 approach. The GBD study uses a set of standardized, analytical, and combined approaches.[15] Using a set of predetermined format, all relevant published data from surveys and peer-reviewed literature from standard databases were obtained. All relevant various basic epidemiological and demographical parameters were collected. Such set of minimum inclusion criteria set for OFC have been described previously elsewhere[14], and the same set of definition was used for this study. All relevant publications and surveys from the past till 2016 have been employed to collate the data, data extracted, optimized, and enriched using established mathematical models as described in detail elsewhere.

OFC for this study includes isolated cleft palate, which corresponds to International Classification of Diseases 10 (ICD-10) codes Q35.2, Q35.3, Q35.5, Q35.6, Q35.7, Q35.8, and Q35.9, and cleft palate with or without cleft lip, which corresponds to ICD-10 codes Q36.0, Q36.1, Q36.9, Q37.1, Q37.5, Q37.8, and Q37.9.[14]

Collating a national level data from existing systematic review of literature (of locoregional studies) aims to compute an aggregate measure of the OFC. However, such an approach is riddled with larger degree of heterogeneity in the prevalence and burden of OFC. Such heterogeneities may arise due to differences in characteristics of the studies (methodological diversity) or study populations (clinical diversity). Logically to address this issue, would be to take statistics to Bayesian concepts. Using this approach, it would be easier to characterize the possible distributions of errors and tackling problems that may arise due to the variations and artificial assumption.[16] All collated data were combined to a single approach using the Bayesian meta-regression tool DisMod-MR 2.1.16, (Disease Modeling Meta-Regression Tool-2, Free tool, Jan Barendregt, Department of Public Health of Erasmus University, Netherlands, Available from www epigear.com). This system encompasses a series of alternative approach, as published earlier.[14] The present study was performed for India and estimates for 2016 are presented. Detailed results from GBD 2016 can be explored to identify basic combined burden parameters in dynamic data visualizations.[17]

In cases of nonavailability of data, GBD applies a nonlinear mixed effect model that employs the relationship between key covariates of the diseases, rate of OFC burden (expressed as per 100,000 population) and performs a spatiotemporal regression as well as Gaussian Process regression. In these cases of nonavailability of pertinent data, including no or minimal observed or expected data, this approach borrows the strength derived from the past data or with that of the neighboring countries with such data. All previous published pertinent data and their definitions are described in detail elsewhere.[18] A number of data points from several past years were identified and the collected data were used in this study from several sources studies. All computations in GBD 2016 were performed 1000 times, with each attempt drawing from the distribution of the sampling error of data inputs. The uncertainty of data corrections for measurement errors, the uncertainty in coefficients from model fit, and uncertainty limits for a quantity of interest were defined by the 25th and 975th value of the ordered 1000 estimate values, expressed as the 95% uncertainty interval (UI).[14] The UI lists the distribution of errors from 1000 times in ascending order and the value between the 25th to 975th time gives us the UI.[14]

The data were then modeled using DisMod-MR 2.1 accounting for visualizing the postadjusted incidence and prevalence besides other data of epidemiological value. From the further specialized tool,[19] the details of the prevalence were collected after adjusting for all covariates, outliers, and input data variations. This utilizes a log rate model of disease prevalence, incidence, remission, and case-fatality rates and fits models with a randomized Markov-Chain Monte Carlo algorithm. This model accounts for all possible outcomes and its probabilities, then incrementally performing risk analysis as mentioned earlier. The model accounts for fixed and random factors.[14] Like any model analysis, the GBD regression analysis also has random and fixed effects which is described by the parameters such as β and its exponentiated forms. The statistical calculation model of GBD exhibits the significant effects both in β and exponentiated β format along with 95% Uncertainty Interval, which is equated to odds ratio of inferential statistical procedure. The modeling strategy and further details are given elsewhere.[14]

Assumptions in the study model

"The DisMod-MR model for OFCs had random effects on prevalence limited to ± 0.5 owing to variation in rate of birth prevalence with clefts. The present model settings permitted to increase smoothness on both excess mortality rate and remission (maximum Xi = 5.0) to fit steep changes in the rates mortality and remission during the first few years of life. Incidence was set to zero for all ages. Remission (cure or dissolution) was set to zero for the first 3 months of life, as cleft lip and/or palate are rarely corrected in the first few months of life. A maximum remission of 0.8 was set for ages 3 months to 2 years, the age range in which cleft repair is most commonly performed, allowing up to 75% of cleft cases to be repaired between 3 months and 2 years of age. Remission was bounded from 0 to 0.07 for ages 2–5 years, 0–0.004 for ages 5–20 years, then bounded from 0 to 0.002 for ages 20–50 years, and set at 0 for ages 50 years +. These limits on remission reflect our priors that up to 20% of remaining cleft cases are repaired between 2 and 5 years of age, another 5% may be repaired between 5 and 20 years of age, and a maximum

5% of remaining cases are surgically repaired between ages 20 and 50 years. Priori (based on theoretical deduction rather than empirical observation) on excess mortality rate were set at a maximum of 2.5 for the early neonatal period, 0.9 for the late neonatal period, 0.24 for the rest of the 1st year of life, 0.05 for ages 1–5 years, and was set to 0 for ages after 5 years. These limits on excess mortality reflect our priori that up to 5% of individuals with OFC die in the 1st week of life, up to 5% die in the following 3 weeks, up to 20% die in the next 11 months, another maximum of 20% before 5 years of ages, and a maximum of 5% of the remaining individuals die between ages 5 and 10 years. During model development, all birth registry prevalence values below 2/10,000 were excluded as outliers, as these data are considered low enough to indicate severe underreporting in the input data."[14] The lists of covariates are discussed in the source document.[14]

OFC can be successfully treated by surgery, often done during the first few months or years of life, but occasionally, later in certain developing countries.[14] For the purpose of interpreting this study, it is assumed that all cleft patients were treated with surgery. The sequelae associated with OFCs are disfigurement level 1 and disfigurement level 2. Level 1 is a slight, visible physical deformity that others notice, which causes some worry and discomfort and disfigurement level 2has a visible physical deformity that causes others to stare and comment. As a result, the person is worried and has trouble sleeping and concentrating. No other outcomes were considered for this study. In addition, a proportion of the population with OFCs is considered to be asymptomatic. The proportion of cleft cases with associated speech problems was calculated following a review of available literature on OFC health outcomes.[14]

We employed the DALYs, years lost to disability (YLDs), and years lost to death (YLL), to assess the overall impact of OFC on the Indians. The definitions used in the GBD can be accessed at Table 1. Furthermore, to study the extent of disability caused by OFC, disability weights were applied. These weights were obtained from a global population survey. Further details can be had from http://ghdx.healthdata.org/gbd-2016. This approach ensures that OFC burden is a function of public perception about disease severity rather than interpretation by health care personnel.[14]

The birth prevalence of OFC for India was collected.[18] From previously published literature,[20] the unmet treatment need for mid-year 2014 derived projections and added another 5% as per the methodology to compute the 2016 projection including untreated palate and lip OFC. This estimate was used to make the unmet surgical need of the population.

Results

From 18 data sources, 70 data points were collated (Supplementary File-1) and subjected to the analysis using the DisMod-MR 2.1.16. Table 2 gives the OFC burden parameters. A total of 0.033% of the Indian population suffers from OFC. It is estimated that in a population of nearly 1.34 billion Indians, 423,519 (373,440–478,776) suffer from OFC. It was made by an estimated 226,882 (2,000,001–2,555,986) males and 196,637 (172,844–221,898) females. In 2016, the estimated prevalence rate/100,000 was 33.27 for males, 31.01 for females, and 32.18 combined for both genders. It was estimated that for all ages, the DALYs lost were 2.05 for 100,000 males, 2.66 for females, and

Table 1: Definitions Used in the present Study. [Confirming to Global Burden of Diseases, 2016]

Term	Definition
Prevalence	The total number of cases of a given disease in a specified population at a designated time. It is differentiated from INCIDENCE, which refers to the number of new cases in the population at a given time.
Incidence	The number of new cases of a given disease during a given period in a specified population. It also is used for the rate at which new events occur in a defined population. It is differentiated from prevalence, which refers to all cases, new or old, in the population at a given time.
Rate per 100,000	This estimate shows in a single country-year-age-sex, the deaths due to cause X divided by the population.
Disability weights	Numerical representations of the severity of health loss associated with a health state. Derived from a worldwide, cross-cultural study to compare the relative severity of health problems, disability weights are numbers between 0 and 1 that are multiplied by the time spent living with a health loss to determine the years lived with disability associated with the cause of that loss.
Disability-adjusted life years (DALYs)	The sum of years lost due to premature death (YLLs) and years lived with disability (YLDs). DALYs are also defined as years of healthy life lost.
Years lived with disability (YLD)	Years of life lived with any short-term or long-term health loss.
Years of life lost (YLLs)	Years of life lost due to premature mortality.
Remission (as a rate)	The number of cases that resolve or are cured per person-year
Standardized mortality ratio (as a rate ratio)	The mortality rate in the diseased compared to the mortality rate in the entire population
Relative risk (as a rate ratio)	The mortality rate in the diseased compared to the mortality rate in the non-diseased population
Excess mortality rate (expressed as a rate)	The number of excess deaths per person-year among prevalent cases
Cause-specific mortality rate (expressed as a rate)	The number of deaths due to the condition per person-year among the entire population; equivalent to prevalence multiplied by excess mortality

Adapted from http://www.healthdata.org/data-visualization/epi-viz

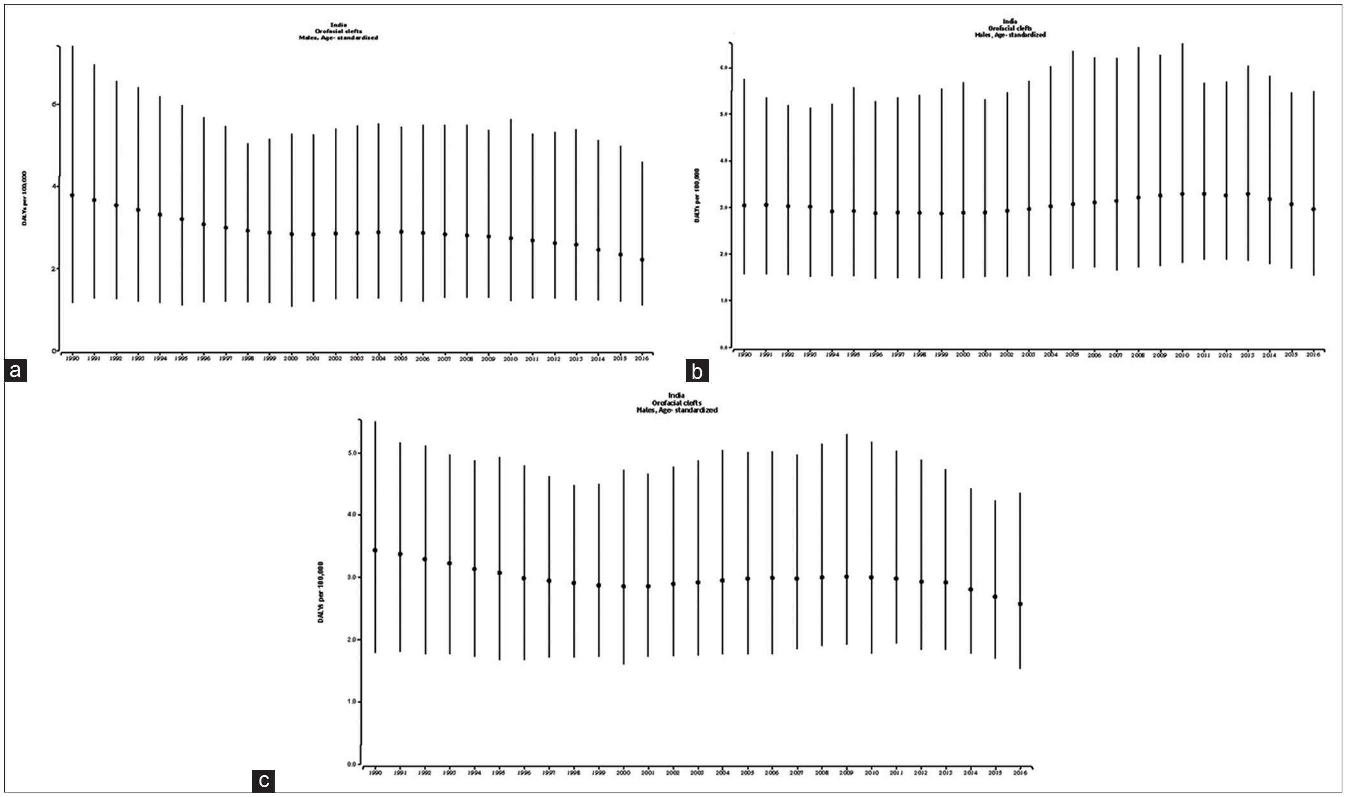

Figure 1: Burden of Orofacial Clefts in India 1990–2016 as Disability-Adjusted Life Years per 100,000, age standardized. (a) Males, (b) Females and (c) both genders

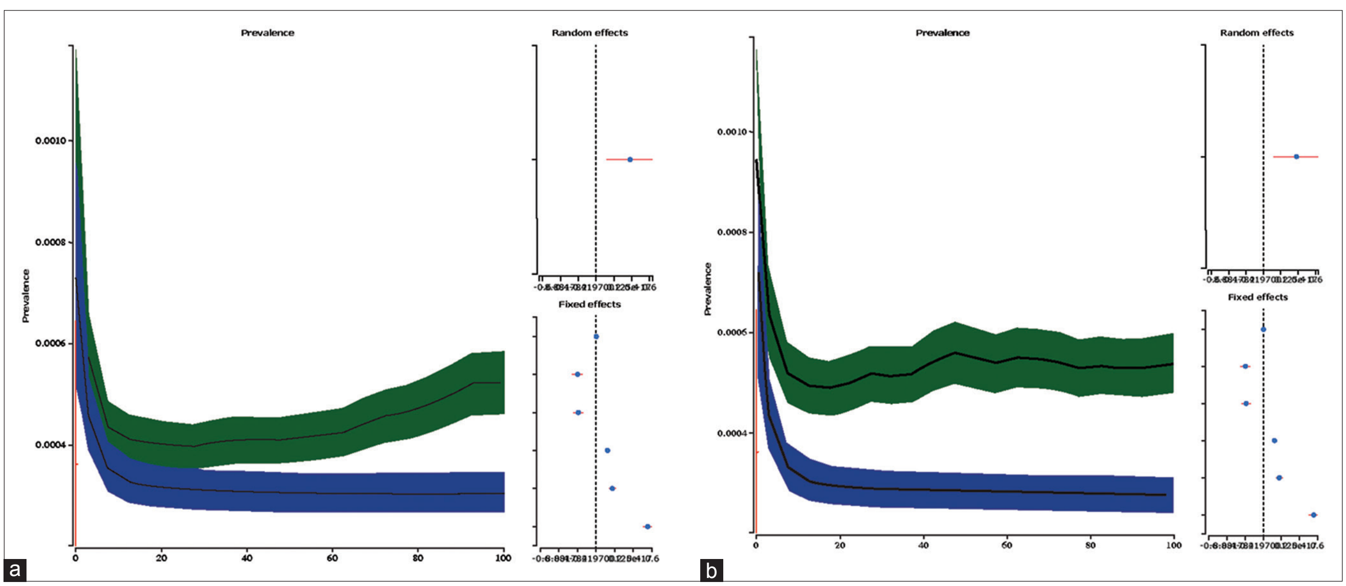

Figure 2: India-specific Orofacial Cleft Prevalence Model age-wise, 2016. (for effects, refer to Table 3) (a) Males (b) Females

2.34 for combined. From 1990s till 2016, the DALYs rates progressively decreased [Figure 1a-c]. It was estimated that deaths due to OFC was 0.017/100,000 males, 0.024 for females, and combined it was 0.02. Most of the OFC burden was borne by the under-five age group, more commonly by the males. However, the DALYs were more considerably affected in the females than the males while DALYs rate/100,000 persons affected children below 5 years of age. A substantial YLL was observed in children below 5 years, which is more in the >5 years age group females [Table 2].

The mathematical model includes the preset assumptions described earlier. With the approach of GBD 2016, India had a higher odds ratio or exponentiated β of 1.46 (1.12–1.88) as compared to global levels. Although β for underreporting was

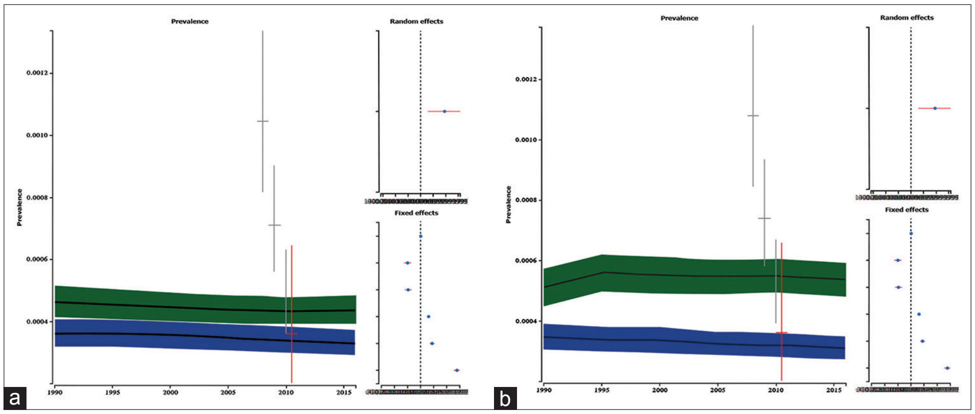

Figure 3: India-specific Orofacial Cleft Prevalence Model, 1990–2016. (for effects, refer to Table 3 (a) Males (b) Females

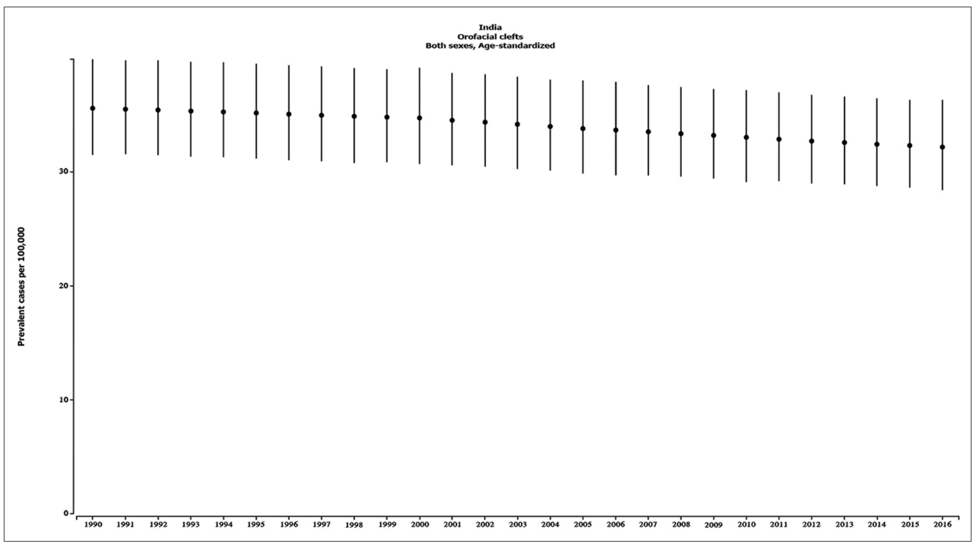

Figure 4: India-specific Orofacial Cleft Prevalence rate (per 100,000 population), age standardized, both sexes 1990–2016

a small number, assumptions and calculations of odds ratio for India were equal to global levels. Similarly, chromosomal diagnoses excluded diagnosis, hospital data (for >1 and <1 ages), gender, and stillbirth were marked significant. The β and odds ratio with 95% confidence interval of all the India-specific models are described in detail in Table 3. Of this, nation was only the random factor and others were fixed factors [Table 3]. The prevalence model for 2016 based on age and gender along with factors are described in Figure 2, while Figure 3 describes the change of the prevalence pattern from 1990 to 2016. The prevalent rates for age-standardized for both genders from 1990 to 2016 are shown in Figure 4.

The mortality rate in the OFC compared to the mortality rate in the nondiseased population expressed as a rate ration, known as relative risk is shown in Table 4 and Figure 5. Gender shows significant difference with females showing less risk than males. However, the model shows no significant random or fixed effect. Remission, as defined in the confines of this study, indicates that the rates are equal to the global pattern and no significant discrepancy exists between genders [Figure 6]. Other epidemiological burdens by gender in Indian OFC are shown in Table 4. The standard mortality rate difference in genders at India and global levels are shown in Figure 7. Figure 8a shows the birth prevalence (as a proportion) in 2016 with India showing an OR of 0.48 (1.56–1.65) and fixed factor of nonrecording 0.83 (0.15–6.63), underreporting 0.97 (0.88–1), gender 1.09 (1.02–1.16), chromosomal diagnoses included 1.22 (1.22–1.22), and stillbirth 1.22 (1.22–1.22). Figure 8b shows the year-wise comparison of at-birth OFC prevalence in India (blue) and global occurrence of OFC from 1990 to 2016. The prevalence model heterogenicity, Zeta 1 (Z1) was 0.25 (0.25–0.26), and in exponentiated form, it was 1.29 (1.28–1.29). The remission model smoothness, xi was 4.14 (3.16–4.95) and exponentiated was 62.88 (23.55–141.03).

An estimated 72,637 cases of OFC were estimated to be living in India with unmet treatment in mid-2014.[20] Using the GBD 2016 approach,[21] the prevalence of >1 year in the remaining years was estimated. The prevalence of OFC in 2014 (below-1 year) was 15,700 in 2014, 15,141 in 2015, and 14,709 in 2016, totaling about 45,550. By the previous model calculation, on average 15% of the 45,550, that is, 6833 would not have access to treatment. Calculating the total

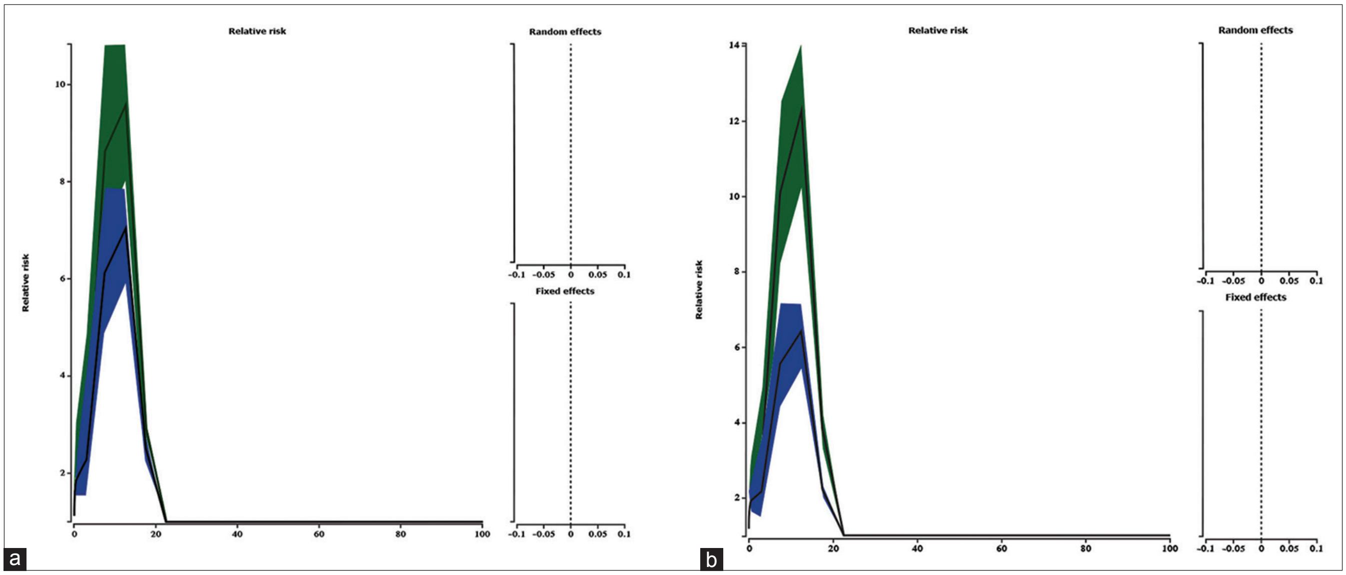

Figure 5: Relative risk model of India-specific Orofacial Clefts, 2016 (for effects, refer to Table 3. (a) Males (b) Females

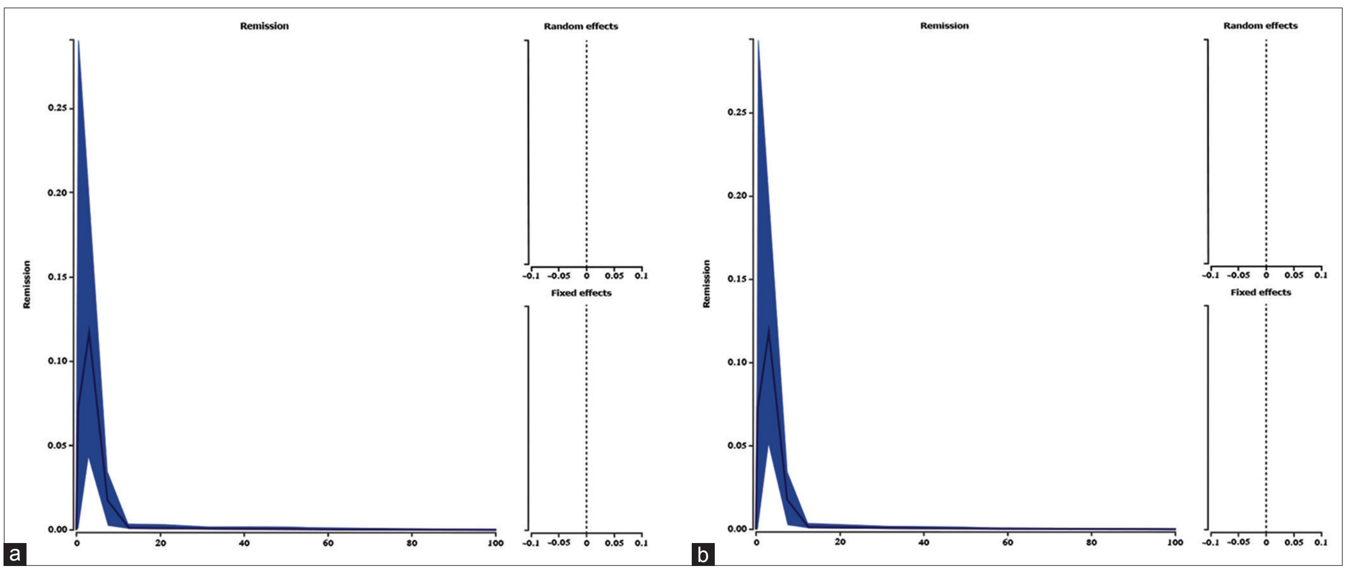

Figure 6: Remission model of India-specific Orofacial Clefts, 2016 (for effects, refer to Table 3). (a) Males (b) Females

unmet cleft treatment need would be 79,430 or 18.76% of all cleft population with OFC were living with untreated clefts.

Discussion

Within the confines of the model parameters,[14] the burden of Indian OFC has been presented. Globally, the prevalence rate of OFC was suggested to be 1.5/1000 live births, while the present study estimates that age-standardized rates of either gender of people living with OFC in 2016 are estimated at 48.57 (95% UI-43.69–53.66)/100,000 population while the same in 1990 was 48.76 (43.14–54.58).[5] The difference is probably due to the estimates. The present study estimates the number of people living with OFC while the earlier reports concerns live births. The birth level comparison from the present study is given in Figure 8. The basis of this data is record obtained from the International Clearinghouse for Birth Defects Surveillance and Research (http://www.icbdsr.org) whose authenticity cannot be disputed.

In this study of 2016, the prevalence of OFC in India was estimated at 32.18/100,000 persons. Recent meta-analysis of hospital-based surveys estimated the prevalence to be 1.3/1000 total births or 130/100,000 per total births.[10] The huge difference could be difference in the approach and parameters used. The present study estimated the prevalence of people living with OFC based on community surveys while the meta-analysis is based on hospital-based surveys for OFC at birth and not at population level. Furthermore, the meta-analysis study warned of overestimation of prevalence, based on their study approach. The discrepancy in the numbers warrants further exploration and detailed study.[10] However, other reports cite annual birth prevalence of OFC in India at

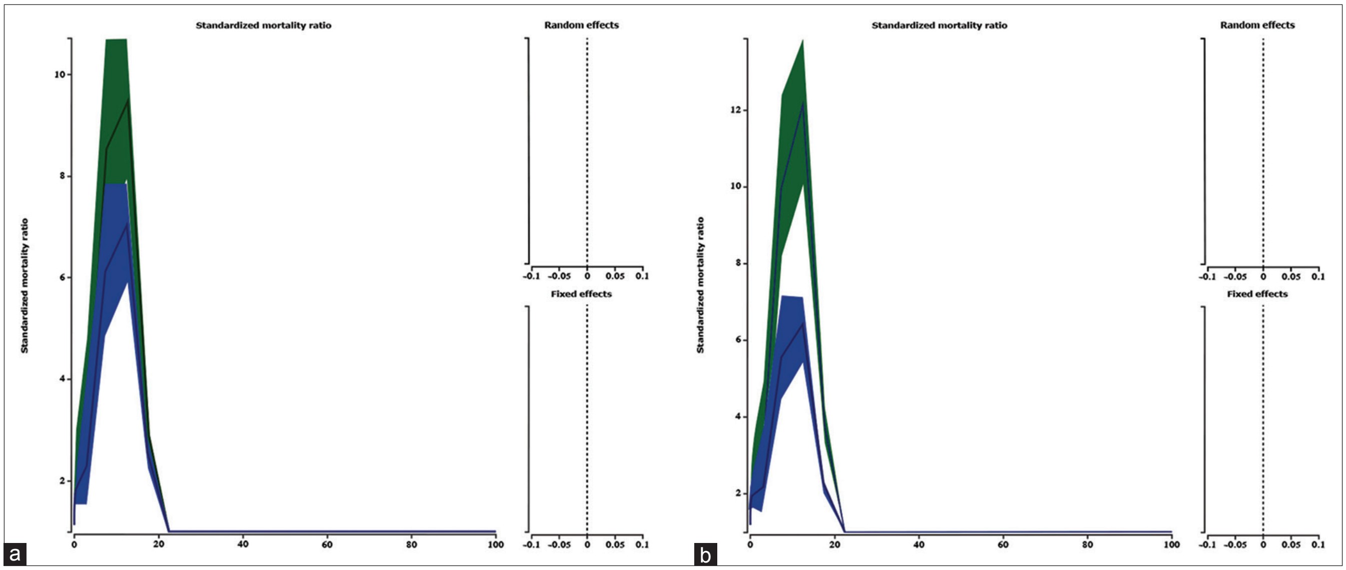

Figure 7: Standardized mortality ratio model of India-specific Orofacial Clefts, 2016 (for effects, refer to Table 3). (a) Males (b) Females

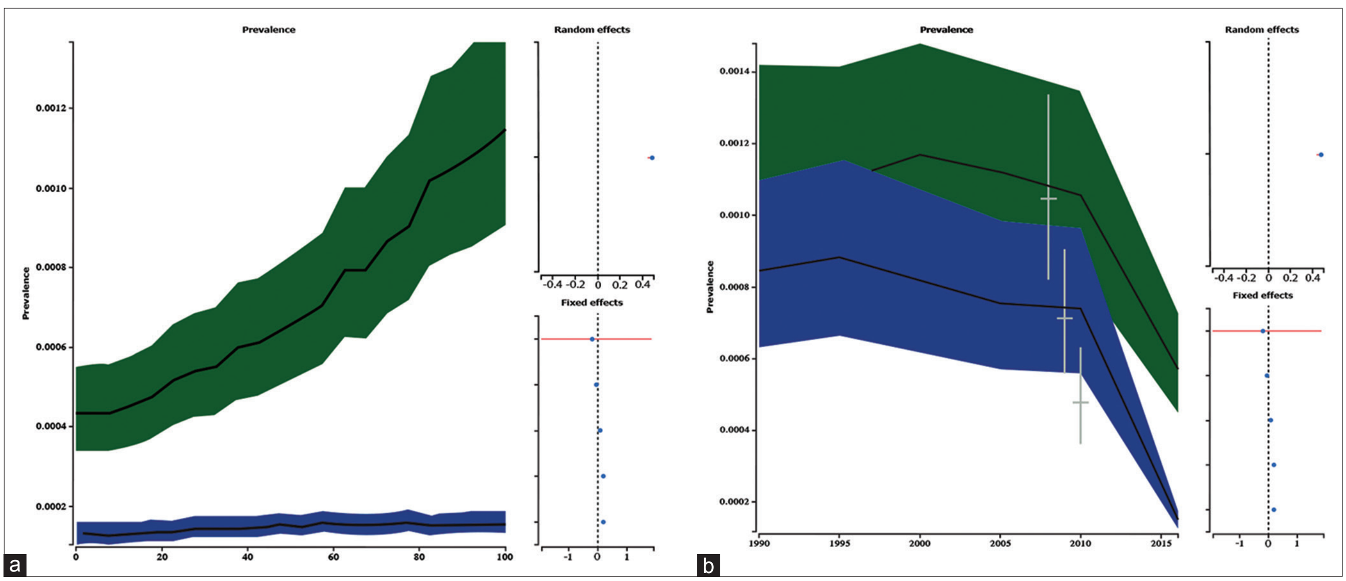

Figure 8: Indian Birth Prevalence of Orofacial Clefts (for effects, refer to Table 3). (a) age-wise, 2016 (b) 1990–2016, year-wise (gray intersects shows timeline of specific published data used in the model).

27,000–33,000/year that is comparable to present result. The difference could emanate from the approach between the studies.[4] In addition, the lack of data from India highlighted earlier should be considered while interpreting the results of this mathematical model based study.[1,4,6]

The mortality rising due to OFC is given in Table 2. The standardized mortality ration and relative risk (as defined in Table 1 and confines of mathematical model assumptions)[14] are higher for males than females and the cause for which needs to be studied in detail. The difference in gender was in agreement with a previous study where a slight male predilection was noticed.[22]

The Lancet Commission on Global Surgery in 2015 indicated that >95% of population in South and Southeast Asia that includes India lacks access to surgical care. The report also signifies the fact that the access to surgical care was inequitably distributed. The near absence of access in many low-income and middle-income countries represents an emergency health crisis, which warrants immediate attention and help of the global health community.[23]

GBD 2016 studies assumed that all OFC were treated. In reality, it is identified that 18.76% of Indian OFC are not treated.[20] From the result of this study and lancet commission report our estimate of about 79,430 people with OFC have or had no access to surgical care. This has to be addressed on a priority basis and appropriate care instituted. The estimated burden of OFC in terms of DALYS as in Table 2 is thus grossly underestimated. The 18.76% of population would suffer from

Table 2: Epidemiological parameters of the Burden due to Oro-facial Clefting in India, 2016

Parameter	Male	Female	Both
Prevalence			
Under 5	29789 (25312-35468)	25669 (21617-30407)	55458 (46861-65810)
5 to 14 years	45730 (39796-52380)	38270 (33183-43779)	84000 (73133-95835)
15 to 49 years	115212 (100826-131171)	98843 (86177-112331)	214055 (187299-243722)
5o to 69 years	29583 (25965-33556)	26898 (23517-30493)	56481 (49601-64277)
Above 70 years	6568 (5769-7444)	6957 (6078-7888)	13525 (11855-15370)
Prevalence, rate per 100,000 persons			
Under 5	50.477 (42.89-60.10)	48.316 (40.69-57.24)	49.454 (41.79-58.69)
5 to 14 years	34.204 (29.77-39.18)	31.949 (27.70-36.55)	33.138 (28.85-37.81)
15 to 49 years	31.097 (27.21-35.41)	28.952 (25.24-32.90)	30.069 (26.31-34.24)
5o to 69 years	30.423 (26.70-34.51)	28.287 (24.73-32.07)	29.367 (25.79-33.42)
Above 70 years	30.517 (26.80-34.59)	28.198 (24.63-31.97)	29.278 (25.66-33.27)
DALYs (Disability-Adjusted Life Years)			
Under 5	10437 (4142-24833)	13827 (6232-27520)	24264 (12595-44321)
5 to 14 years	816 (521-1204)	683 (434-1004)	1499 (956-2209)
15 to 49 years	2057 (1320-2984)	1764 (1128-2575)	3821 (2441-5556)
5o to 69 years	528 (338-767)	480 (307-700)	1008 (642-1471)
Above 70 years	117 (75-170)	124 (79-181)	241 (154-352)
DALYs, Rate per 100,000 persons			
Under 5	17.686 (7.02-42.08)	26.027 (11.73-51.80)	21.637 (11.23-39.52)
5 to 14 years	0.611 (0.39-0.90)	0.570 (0.36-0.84)	0.592 (0.38-0.87)
15 to 49 years	0.555 (0.36-0.81)	0.517 (0.33-0.75)	0.537 (0.34-0.78)
5o to 69 years	0.543 (0.35-0.79)	0.505 (0.32-0.74)	0.524 (0.33-0.76)
Above 70 years	0.545 (0.35-0.79)	0.503 (0.32-0.73)	0.523 (0.33-0.76)
Years of Life Lost			
Under 5 years	9905 (3618-24419)	13369 (5757-27046)	23274 (11634-43280)
Years Lived with Disability			
Under 5	532 (337-799)	458 (291-683)	990 (626-1483)
5 to 14 years	816 (521-1204)	683 (434-1004)	1499 (956-2209)
15 to 49 years	2057 (1320-2984)	1764 (1128-2575)	3821 (2441-5556)
5o to 69 years	528 (338-767)	480 (307-700)	1008 (642-1471)
Above 70 years	117 (75-170)	124 (79-181)	241 (154-352)
Death, numbers			
Early neonatal	60.2 (18.69-154.55)	74.7 (26.99-176.91)	134.9 (61.50-265.74)
Late neonatal	15.4 (4.98-43.48)	34.2 (12.74-72.10)	49.6 (22.39-98.47)
Post neonatal	37.3 (12.73-100.67)	36.7 (14.70-85.09)	74.0 (35.51-155.92)
1 to 4 years	1.8 (0.47-5.27)	9.1 (2.63-29.44)	10.9 (4.16-31.29)

Table 3: Model parameters that was significant in the burden of orofacial clefting in India

Model	Parameter	Beta	Exponentiated Beta (95% UI) or Odds ratio (95% CI)
Random	Country-India	0.38 (0.12-0.63)	1.46 (1.12-1.88)
Fixed	Under reported	0.0016 (0.00003-0.0054)	1 (1-1.01)
	Chromosomal diagnoses excluded	-0.2 (-0.24-0.17)	0.82 (0.79-0.85)
	Hospital data for under-1 age group	-0.19 (-0.24-0.14)	0.82 (0.79-0.87)
	Gender	0.12 (0.1-0.014)	1.13 (1.11-1.15)
	Still birth	0.18 (0.14-0.21)	1.19 (1.15-1.24)
	Hospital data for over 1 year only	0.56 (0.5-0.61)	1.75 (1.66-1.84)

high DALYs owing to living with untreated cleft[12] and would increase manifolds if all sufferings of untreated OFC including psychological, improper speech, and financial well-being. In addition, the GBD approach only accounts for the DALY, YLL, and YLD for the patient and not account for the burden experienced by the caregivers and careproviders.[23] Together, the burden of DALYs, YLD, and YLL of treated and untreated OFC in India would increase several folds. Yet, the robust estimates mentioned in Table 2 are higher and warrant deeper study.[13,23] Even among the treated, within the confines of

Table 4: Epidemiological parameters of burden of orofacial clefting in india, 2016 age standardized

Parameters	Males	Females
Remission, rate	0.012 (0.0061-0.018)	0.013 (0.0068-0.019)
Standardized mortality ratio	2.19 (1.98-2.42)	2.06 (1.88-2.26)
Excess mortality rate	0.0031 (0.0024-0.0041)	0.0035 (0.0027-0.0046)
Relative risk	2.19 (1.98-2.42)	2.06 (1.88-2.26)
With condition mortality rate	0.02 (0.019-0.021)	0.018 (0.017-0.019)
Cause specific mortality rate	0.0000015 (0.0000011-0.0000022)	0.0000017 (0.0000013-0.0000024)

the GBD 2016 mathematical model and assumptions, it is revealed that a substantial number of cases are not satisfied with their surgical outcome and feel inadequate. This has to be investigated further. The assumptions for this as mentioned in the material section exceed ground reality.

Surgery for cleft lip/palate is generally perceived to be costly and imparts a huge economic burden on the family.[5]

The Lancet Surgery Commission in 2015 identified that from public health point of view, cleft lip/palate median cost-effective ratio CERs of the cleft lip, or palate repair US $47·74 per DALY averted. The same commission identified that at hospital-based cleft lip/palate repair in the adjoining country of Nepal US $34.09 per DALY averted.[24] With the same cost estimation in India and the fact that nearly 18.76% of OFC have not undergone surgical correction, a simple estimation for "unmet" OFC burden, adds a significant cost to a health system that is already burgeoned with communicable and noncommunicable diseases.

Cleft missions are known to strengthen the host country's existing health systems through the development of surgical infrastructure, training of local workforce, and provision of financial sustainability. India has a strong tradition of cleft repair and drastic improvement in its cleft rehabilitation programs. In spite of the same, the huge burden of untreated and "unmet" needs of OFC is worrisome. The policymakers need to address the issue to enable all untreated OFC to be corrected.[24]

Literature cites that Indian children, in spite of OFC surgical treatment, the psychosocial trauma remains high.[25] Hence, there is still huge unmet treatment need existing even in the OFC-treated population in terms of speech training/esthetic concern/psychosocial domain. There is a dire need of more studies focused in this group to estimate the wholesome burden of OFC in treated children/adults.[25-28] The direct and indirect economics of OFC is quite high, and India-specific studies need to be drawn. Although direct field level calculation of the cost of met and unmet OFC is nearly impossible, mathematical modeling of costs is possible based on findings in the literature.[12,29] Future modeling studies need to incorporate the costs incurred by caregivers, long-term speech rehabilitation, and possibility of support needs of discontent arising from treated OFC in terms of speech and self-perception.

The study suffers from poor data representativeness that emanates from lack of sufficient studies from India. Other non-consideration of only residual, postsurgical concerns of patients and not the caregiver burden in OFC and assumption that all OFC are treated surgically forms significant drawback.[14] The limitations also include the assumptions in the model and nonconsideration of rural–urban divide, access to surgical care, postsurgical care, and role of socio-religio-cultural context. The exact role of predisposing factors such as folic acid deficiency, effect of smoking tobacco, other micronutrient deficiency, and microbial infections on the India-specific model has to be studied further beyond the confines of the present mathematical model.[4,5]

Conclusions

The present mathematical model study based on GBD2016 presents a relatively lower prevalence and incidence rate of OFC in the population than the previous estimates. Furthermore, the present study highlights that the OFC prevalence and its burden (in terms of epidemiological parameters) are steadily decreasing. The results of the combined efforts to reduce the burden of OFC in India are fetching desired results. Yet, owing to the larger population, a substantial number of persons still suffer from OFC whose quality of life needs a larger surgical/medical intervention. The robust estimate presented here could help the policymakers and health professionals to make meaningful efforts in eradicating OFC in the future.

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Conflicts of interest

There are no conflicts of interest.

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