

# Cleft craniofacial care in Asia—a narrative review

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**Background and Objective:** A 2002 World Health Organization (WHO) report was published arising from the two-part meeting held in Geneva, Switzerland [2000] and Park City, Utah, USA [2001] on global strategies to reduce the health-care burden of craniofacial anomalies as part of WHO's Human Genetics Programme. How are those strategies working out in cleft and craniofacial care in Asia two decades on?

**Methods:** Articles are searched from PubMed using MeSH terms “Cleft Lip and Palate Treatment”, “Asia”, “South East Asia”, “East Asia” and from the public domains for Chinese articles using key phrase “中国唇腭裂”. More relevant articles are further found from the list of references in the studies.

**Key Content and Findings:** Cleft care in Asia has progressed in the last two decades through the action of non-profit, non-governmental cleft organisations comprising of healthcare professionals, health administrators, philanthropists, volunteers as well as cooperation from local governments to provide surgical and health access to underserved populations. The mission model has gradually evolved into a more sophisticated foundation-based model with the aim to set up sustainable comprehensive cleft centres (CCCs) for the local population. More efforts need to be channelled to the west and central Asian countries as cleft protocols get more established in the south, south-east and east Asia.

**Conclusions:** The environment is set up for closer regional collaboration through a multicentre Asiacleft study in the near future. However, there is a need for more standardisation of data collection methods and cleft management protocols.

**Keywords:** Asiacleft; cleft lip; cleft palate; cleft lip and palate; Asia

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## Introduction

### Background

A 2002 World Health Organization (WHO) report was published arising from the two-part meeting held in Geneva, Switzerland [2000] and Park City, Utah, USA

[2001] on global strategies to reduce the health-care burden of craniofacial anomalies as part of WHO's Human Genetics Programme (1). The key areas of focus: (I) evidence-based care—(i) quality improvement which includes adopting an international set of guidelines for the provision of clinical services and for the maintenance of a minimum clinical

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**Table 1** The search strategy summary

Items	Specification
Date of search	30 Nov 2022
Databases and other sources searched	PubMed, Internet
Search terms used	“Cleft Lip and Palate Treatment”, “Asia”, “South East Asia”, “East Asia”, “中国唇腭裂”
Timeframe	1993–2023
Inclusion and exclusion criteria	Include all searchable articles relevant to cleft care in Asia according to the focus areas from the WHO 2002 report on global strategies to reduce health-care burden of craniofacial anomalies
Selection process	WWL, CKC

WHO, World Health Organization.

record; (ii) access and availability to adequate levels of care. (II) Gene/environment interaction—(i) epidemiology; (ii) etiology; (iii) research and prevention.

About a decade following this report, Professor William Shaw, the then director of the WHO Collaborating Centre in Craniofacial Anomalies reported that the global cleft efforts were still a work-in-progress with mixed successes in improving services and evidence base (2). In his words, “*Cleft lip and palate remains an orphan condition, falling between a variety of clinical disciplines, and often forgotten by public health consultants and health commissioners*”. How are those strategies working out in cleft and craniofacial care in Asia since then?

### Rationale and knowledge gap

There is currently no overview report on the orofacial cleft management in Asia to the authors’ knowledge. Most if not all of the available publications are related to (I) prevalence and etiologies of orofacial clefts or (II) management of orofacial clefts within individual countries or regions. Geographically, Asia may be divided into 5 regions: Central, West, South, East and South East. It is the largest, most populous and ethnically diverse continent. The average global incidence of cleft lip with or without cleft palate is 1 in 600–700 births and in Asia there is an estimated 100,000 births with cleft lip and palate annually. Babies born with orofacial clefts face a host of issues including eating, speaking, breathing, and hearing challenges together with their associated problems like undernutrition in babies, learning disabilities, and psychosocial effects on individuals due to their appearances. The Lancet Commission on Global Surgery 2030 together with other studies (3–6), highlighted the need for more surgical services to tackle untreated diseases and conditions that would result in

unrealised economic gain and/or economic burden due to the conditions. It is estimated that 5 billion people worldwide do not get adequate access to timely and affordable surgical and anaesthesia care and such a burden is most felt in low income and low-middle income countries (LMIC). In South-East Asia, more than half of the countries in the bloc are listed in the World Bank’s list of LMICs. The potential economic benefit to these countries has been calculated to be US\$16.1–42.3k per individual with an expense of US\$328–820 for the disability-adjusted life years averted (7).

### Objective

This narrative review aims to give an update on cleft and craniofacial care in Asia in the past two decades. We present this article in accordance with the Narrative Review reporting checklist (available at <https://fomm.amegroups.com/article/view/10.21037/fomm-23-8/rc>).

### Methods

The search strategy is summarised in *Table 1*.

The theme of this review relates to the key areas of focus arising from the 2002 WHO report on global strategies to reduce the health-care burden of craniofacial anomalies: (I) evidence-based care—(i) quality improvement which includes adopting an international set of guidelines for the provision of clinical services and for the maintenance of a minimum clinical record; (ii) access and availability to adequate levels of care. (II) Gene/environment interaction—(i) epidemiology; (ii) etiology; (iii) research and prevention. Articles describing health care economics, epidemiology, treatment strategies and research efforts surrounding cleft care were reviewed. Articles were searched from PubMed,

Medline, Embase and Google Scholar using MeSH terms “Cleft Lip and Palate Treatment”, “Asia”, “South East Asia”, “East Asia” and from the public domains for Chinese articles using key phrase “中国唇腭裂”. For studies reporting of prevalence of cleft deformities, the search terms “cleft prevalence” followed by the Asian country, e.g., “in China” were used. More relevant articles were further found from the list of references in the included articles. In addition, any non-scholarly articles that were relevant to cleft care in Asia were also referenced.

## Discussion

### *Cleft care models*

#### **Comprehensive cleft centre (CCC) model**

In Asia, varying models of cleft care exist. The CCC model is found in countries or cities where their populations have greater accessibility to comprehensive medical facilities. Correction of the cleft lip and palate deformity with good clinical outcomes requires timely interventions by a multidisciplinary team from an individual’s birth to adulthood. The CCC model is a team-based approach involving a team of medical, dental, allied health specialists with administrative support in managing cleft deformities (8). The Eurocleft studies compared inter-centre outcomes and determined best practices and protocols in cleft management. The studies showed that the best cleft care outcomes tend to be found in centralised referral centres that managed cleft deformities in high volumes (9-13). In the next decade, cleft care resources in some developed countries and cities were reorganised and consolidated while others remain fragmented with some smaller centres reporting little chance of having sufficient subjects for clinical trials due to the decentralised provision of cleft care (2). Some of the obstacles preventing the creation of a dedicated centralised cleft referral centre include lack of involvement from the health authorities in organising cleft care and unwillingness of professional groups to give up the small patient load for various reasons.

In Asia, CCCs can be found in larger cities, e.g., The Center for Cleft Lip and Palate, No.9 Hospital, Medical College, Shanghai Jiao Tong University, in city states with high accessibility and availability of surgical care services, e.g., Cleft and Craniofacial Centre KK Women’s and Children’s Hospital, Singapore or in institutions that have benefitted from the transfer of expertise knowledge and funding through partnerships with international

non-government organisations (NGOs) and foundation/charities, e.g., Smile Asia, Singapore; Noordhoff Craniofacial Center at Chang Gung Memorial Hospital.

#### **The mission model**

LMICs present many underserved areas in cleft care. Humanitarian relief efforts in the form of medical mission trips answer to these unmet surgical and healthcare needs of the population to whom the local governments may have limited resources to care for. The scale of such mission efforts varies in terms of geographical location, delivery model, services provided and sustainability of the effort (14-18). While short term cleft missions provide availability to surgical treatment for populations who have no such access previously, many have recognised the weakness of long term follow up and continuity of care (19). Smaller missions may be limited in resources and sustainability which limits the ability to assemble a comprehensive care team. Such limitations have been correlated to higher complication rates (20). Some have reported that the post-operative presence of an oronasal fistula is 20 times higher than in cases in high income countries (21-22). Cleft and craniofacial mission care requires plenty of preparation and follow-on work which involve collaborating with multi-agencies and require a multidisciplinary team to ensure that patients get the care that they need (23).

A Cleft 2013 Task Force made up of stakeholders in cleft care from all continents highlighted 3 main goals for missions: (I) provide cleft treatment for patients; (II) coordinate with local staff to begin forming a local team to provide care; (III) disseminating information regarding cleft care to the local population (24). The most recent set of international guidelines on the conduct of cleft mission was published by the World Cleft Coalition (WCC) (25). The WCC was initiated at the 13<sup>th</sup> International Congress of Cleft Lip and Palate and Related Craniofacial Anomalies in Chennai in 2017 and consists of 6 international Non-Governmental Organisations (NGOs)—American Cleft Palate Craniofacial Association, European Cleft Organisation, Global Smile Foundation, Operation Smile, Smile Train and Transforming Faces. This set of guidelines outline the areas where cleft missions are encouraged to conform to.

The mission model has evolved into a foundation based or partnership model in Asia where it has one of the world’s most concentrated number of cleft organisations (18). The foundation-based missions in LMICs and in countries with regions having poor access to healthcare, generally

have more resources to organise comprehensive cleft care through efficient pooling of volunteer, partnering of local charities and maintenance of manpower to sustain the cleft care efforts in the local population. This is further achieved by training the local healthcare team in cleft care, transfer logistic know-hows to the local administration and support teams and establishing infrastructure and equipment to facilitate accessibility to treatment. Many of these organisations were formed at the start of this century and two decades on, we are starting to see the fruits of such concerted efforts in the reports generated from the data collected (26-29). For example, SmileTrain, the largest cleft charity in the world maintains a standardised database of all patients who have benefitted from their sponsored surgeries and cleft care, thereby allowing them to conduct clinical and research audits to advance cleft care (30). As we see more collaborations between these NGOs we should see increased outreach to underserved areas within Asia (31), more publishing of cleft treatment data and visible downstream impact in health care burden reduction.

#### *Where are we in Asiacleft?*

Asia is home to about 60% of the world's population that is ethnically diverse (32). Looking back at the 2002 WHO report on global strategies to tackle health-care burden of craniofacial anomalies, have we progressed much in two decades according to the themes WHO set out to achieve?

#### **Evidence-based care**

##### *Quality improvement which includes adopting an international set of guidelines for the provision of clinical services and for the maintenance of a minimum clinical record*

With the development of an agreed set of internationally recognized practice guidelines (International Treatment Program Standards) by the WCC (25) we hope to see greater adoption of these practices and quality controls implemented by cleft charities around the world. Surgical safety, quality control, patient education, patient selection, patient follow-up, comprehensive care, partnership with host nation and professionals and training for sustainability and local capacity building are the eight key areas identified in this guideline (25) which are minimum core standards to adhere to and recommended best practices in ensuring safe, comprehensive and sustainable cleft care.

It is a big step in the right direction as this international coalition becomes the main driver forward in quality cleft care provision throughout underserved areas in Asia.

#### *Access and availability to adequate levels of care*

Barriers to care remains an outstanding issue in many LMICs. There is a strong negative correlation between the national income status and delayed access to primary palate surgery remains (33,34). A survey was conducted on the provider's perception on the barriers to cleft care. The barriers identified differs by geography. In Southeast Asia, the main perceived barriers were patient travel cost and patient awareness while in East Asia, lack of financial support, infrastructure and training were the main barriers (35). As cleft charities and foundations continue to empower communities to reduce this health care burden and plugging care gaps which the local government cannot fill, we may be able to see the economic benefits from these surgeries as beneficiaries of these sponsored surgeries will be able to continue to contribute to their countries' national income.

#### **Gene/environment interaction**

##### *Epidemiology*

Cleft prevalence reported around the world varies in terms of the source of data collection (hospital-based versus population-based registries). An estimated prevalence rate reported in Asia is presented in *Table 2*.

The prevalence rates presented in *Table 2* highlight two challenges in cleft epidemiology: (I) the paucity of data in LMICs predominantly in central and southeast Asia; (II) the potential variability in prevalence rates across Asia due to inconsistent collection methods. Asia, being ethnically diverse, can possibly present a varied prevalence across different regions and racial groups, however, due to non-standardised data collection and reporting methods, social, genetic and environmental risk factors are hard to identify definitively. There have been proposals (40,52) to revise classification of orofacial cleft subphenotyping to truly reflect the changing understanding on the etiologies of orofacial cleft. There should also be international consensus on how any revised classification can be used in conjunction with existing diagnosis codes, e.g., ICD10/ICD11 to accurately record the cleft subphenotypes. In addition, harmonisation efforts between commonly adopted classification system should be attempted with the aim to make data more comparable between cleft centres.

In gathering birth numbers to use as the country's denominator for cleft and craniofacial anomalies incidence calculation, the WHO workgroup recommended using population-based registries instead of hospital-based ones with multiple sources of ascertainment to ensure that the

**Table 2** Cleft prevalence in Asia per 1,000 people (36-51)

Country	Prevalence per 1,000 people
China	1.46
South Korea	1.96
Japan	2.0
India	1.3
Pakistan	1.91
Thailand	2.14
Vietnam	1.49
Singapore	1.67
Philippines	1.94
Malaysia	1.24
Saudi Arabia	2.19
United Arab Emirates	0.5
Oman	1.5
Kuwait	1.5
Iran	0.97
Sudan	0.9

derived numbers are as complete as possible. As different cleft deformities may have different etiological associations with ethnic predilection, craniofacial registry should present ethnic groupings during the recording of cleft types and associated malformations.

Accurate cleft registries allow for prevention planning by identifying etiological factors and targeting populations at a higher risk. Such registries tend to be more present in higher income countries (36). As national birth defect registries become digitalised, we predict that epidemiological data will become more accurate in time to come with governments implementing quality control measures (37,38). Continued development in the last two decades in genetic analysis and the use genome-wide association studies on target populations led to the increased number of candidate genes and/or loci discovered. Genome-wide association studies using case-parent trio data derived from international cleft consortiums (Geneva and spin-off projects) (53-55) identified many genes associated with orofacial cleft over the years some with varying ethnic susceptibility and penetrance. These genes have been well summarized and described in studies (56-58).

Through large cohort association studies, gene-

environment interactions in orofacial cleft formation can be reliably defined but many associations currently remain inconclusive. We are hopeful that with increasing clarity of our Asian genetic ancestry and inheritance markers (59) and more standardised cleft data collection, we will be able to identify definitive etiologies of this condition and be able to prevent some of the cases from occurring in the near future.

#### **Research and collaboration**

As more CCCs are established across Asia, the chance of collaboration to develop best practices in cleft care be it surgical techniques or new treatment modalities that reduce long term burden of care for patients increases. For the past twenty years, regular cleft meetings, congress, conferences and workshops provided platforms for various stakeholders to convene to discuss on the future course of the regional and international cleft landscape and the impetus for advancement in cleft care especially in LMICs. These events also serve as a conduit for knowledge transfer and building of regional and international network of professionals.

Some of these events included:

- ❖ The biennial meetings organised by the International Cleft Lip and Palate Foundation (ICPF) with the last being 13<sup>th</sup> World Congress of ICPF held in Nagoya, Japan in 2019;
- ❖ The biennial meetings organised by the Asia Pacific Craniofacial Association (APCA), which is an invite-only society of craniofacial surgeons;
- ❖ The Asian Pacific Cleft Lip-Palate and Craniofacial Congress organised by Australasian Cleft Lip and Palate Inc. (ACLAPA);
- ❖ While many, if not all, face-to-face conferences were cancelled or postponed during the COVID Pandemic period, the Solutions4CCC virtual conference organised by the Circle of Cleft Professionals continued to engage more than 140 participants internationally on Cleft Management through 2020 and 2021. The Circle of Cleft Professionals is a worldwide network of cleft professionals and cleft charity with 11 international NGOs in collaboration with focus in promoting Comprehensive Cleft Care in LMICs. Membership is free and members have access to webinars, discussion forums and resources of continual professional learning.

On research and accessibility to foster active exchange: national cleft associations serve as ambassadors and point of contacts for regional and international collaboration efforts. They are also the organising bodies of cleft conferences when they are held in the host countries. Below are some

of the cleft societies and associations in Asia that also have presence in the public domain:

- ❖ Japan: Japan Cleft Palate Association (<https://square.umin.ac.jp/JCLP/en/index-en.htm>);
- ❖ Korea: Korea Cleft Palate-Craniofacial Association (KCPCA) (60);
- ❖ China: Chinese Stomatological Association (<http://www.cndent.com/wp-content/uploads/2022/01/唇腭裂序列治疗指南.pdf>);
- ❖ Taiwan Cleft Palate Craniofacial Association (<https://www.tcpa.org.tw/>);
- ❖ Thailand: Thai Cleft Lip-Palate and Craniofacial Association. It is noteworthy that the association maintains a network list of experts and their area of specialty by province for ease of reference on their website (<https://thaicleft.org/network>).

### ***Strengths and limitations of review***

This review gave a broad overview on the developments in orofacial cleft research and management in Asia over the last two decades, a perspective that had not been provided until now to the knowledge of the authors. To include all the reports and good works of orofacial cleft workers in Asia in this review will be difficult to fit into the context of this narrative review especially when it comes to the depth of cleft research. Instead, reviews on these topics were referenced with table summaries reproduced in this article.

### **Conclusions**

There is a relative paucity in cleft treatment data in central and west Asia but as more cleft teams from the likes of SmileTrain and SmileAsia reach out to countries like Afghanistan and Uzbekistan, we may see more information on the population in those regions. Existing cleft database should be harmonised across cleft charities and government agencies as far as possible for ease and accuracy of data analytics. Standardisation of reporting of cleft missions and projects are also equally important. A systematic review concluded that cost-analyses comparison between cleft missions were not valid due to the varied methods of cost analysis (61). The review proposed using the WHO-CHOICE standards as a tool for economic evaluation for global health interventions.

The cleft care development is maturing in each of the Asian blocs (south, south-east and east) individually as transference of resources and expertise flow from higher

income regions to resource-constraint areas. Asia is set for collaboration in terms of multi-centre comparison when more CCCs established their protocols conforming to internationally recognized standards in cleft care. At the earliest opportunity, key drivers of national cleft efforts (e.g., cleft associations and organisations) should lead and collaborate with fellow counterparts to set the stage for an Asiacleft study which can create new insights to cleft management and research.

Through the partnership of NGOs with local governments and health administration, there is hope that barriers to surgical and health care can be gradually reduced with patients gaining greater access to quality surgical and health care needed to reduce the disease burden of cleft and craniofacial anomalies.

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