Spotlight on Lung Cancer Disparities in India

Manas Gunani, MD[1]; Rahul Winayak, BSc, MBChB[2,3]; Anisha Agarwal, MD[4]; Aruni Ghose, MBBS[3,5,6,7,8,9]; Rounak Das, GCSE[10]; Kumar Prabhash, MD, MBBS, DM[11]; Vanita Noronha, MD, MBBS, DM[11]; Giuseppe Luigi Banna, MD[12,13]; Stergios Boussios, MD, MSc, PhD, FRCP[7,14,15,16,17]; and Swarupa Mitra, MD, MBBS[18]

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Epidemiology

In 2020, lung cancer (LC) was the second most frequently diagnosed cancer (11.4% or 2.2 million cases) and the leading cause of cancer-related deaths (18% or 1.8 million).[1] Although the incidence and mortality in high-income countries (HICs) are three to four times higher than those in low- and middle-income countries (LMIC), a trend reversal in future is likely, courtesy the evolving tobacco epidemic. In 2016, 80% of individuals age 15 years or older smoking tobacco originated in LMICs, which is projected to increase.[2]

India is the world's second largest tobacco consumer and the third largest tobacco producer. The Global Adult Tobacco Survey in 2016/2017 noted 267 million tobacco users in India, comprising 42.4% men and 14.2% women.[3] Secondhand smoke (SHS) exposure is another major concern, with high prevalence in both workplace and home, among 38.7% and 30.2% of adults, respectively.[4] Despite banning public smoking in 2003, SHS exposure is still common among public areas with varying law enforcement, including bus stops and cinema halls, compared with educational or health care settings with stricter compliance.[5] LC is a leading cancer among Indian men, with a steady rise among both smokers and nonsmokers. Another concerning trend is the rising incidence among women, with domestic SHS exposure possibly contributing[6] (Table 1). This article aims to explore the disparities and challenges in LC care in India and propose potential solutions.

The India State-Level Disease Burden Initiative partners revealed significant variation in age-standardized incidence of the top 10 malignancies, including LC from 1990 to 2016. In men, the crude LC incidence was the highest in Kerala (19.9) and Mizoram (13.1), whereas in women, it was the highest in Mizoram (30.4) and Manipur (12.4).[8] Despite the Northeast having the highest incidence of LC for both sexes, the available health care facilities are inadequate to address this.[9]

Risk Disparities

Patients from lower socioeconomic status (SES) are likely predisposed to poorer prognosis compared with higher SES, primarily due to reduced access to disease management modalities and/or late presentation or medical emergency. For these groups, diagnostic imaging like computed tomography (CT) or positron emission tomography (PET) scans is financially exorbitant, and they are less likely to receive any definitive treatment.[10] Inequalities in education also affect smoking and LC treatment. During 2003-2011, men with less than a high school diploma and living below the poverty line had 2.6 times higher mortality than their educated and affluent counterparts.[11]

In addition to SES, environmental factors such as air pollution are increasingly being correlated with higher risk and poorer prognosis for LC, even in nonsmokers.[12,13] In fact, this risk equates to that of tobacco smoking (43%) in terms of disability-adjusted life years.[14] India was the third most air polluted country with 39 of its cities in the top 50 such cities globally in 2023.[15] A major air pollutant is particulate matter (PM). Exposure to PM2.5 pollutants is linked to an increased risk of lung adenocarcinoma in nonsmokers with *EGFR* mutations.[12] The Indian average concentration of PM2.5 is 10.9 times the WHO-recommended target.[16] The Commission for Air Quality Management commenced in 2021 to tackle high levels of air

TABLE 1. Region- and Gender-Wise Incidence of Lung Cancer in India From 2012 to 2016[7]

S.No.	Registry	Number of Cases (males)	Number of Cases (females)
North			
1	Delhi	3,249	962
2	Patiala district	374	134
South			
3	Hyderabad district	561	262
4	Kollam district	1,833	359
5	Thi'puram district	1,685	545
6	Bangalore	1,335	596
7	Chennai	1,397	555
East			
8	Kolkata	2,040	602
West			
9	Ahmedabad Urban	1,188	311
10	Aurangabad	216	79
11	Osmanabad and Beed	177	93
12	Barshi rural	25	26
13	Mumbai	2,554	1,390
14	Pune	735	449
Central			
15	Wardha district	170	85
16	Bhopal	390	114
17	Nagpur	368	177
Northeast			
18	Manipur	698	649
19	Mizoram	618	528
20	Sikkim	83	73
21	Tripura	1,103	263
22	West Arunachal	79	46
23	Meghalaya	286	116
24	Nagaland	84	37
25	Pasighat	25	9
26	Cachar district	400	125
27	Dibrugarh district	135	52
28	Kamrup Urban	494	181

pollution in New Delhi. Efforts included road sweepers and sprinklers removing dust from major roads, encouraging clean transport via installing electric vehicle charging stations with low usage costs, and introducing newer electric buses.[17]

Access Disparities

India's overall health care expenditure accounts for only 3.6% of its Gross Domestic Product compared with 8.8%, the average of Organisation for Economic Co-operation and Development member countries.[18] Health insurance coverage is inadequate. Only 41% of households (38% and 42% in urban and rural areas, respectively) had any usual member on a scheme, according to the National Family Health Survey 2015-2016.[19]

The cancer care infrastructure remains inadequate in comparison with the population and patient density. Although the financial burden per patient with cancer is one of the lowest documented ($641 *v* $86,758 US dollars [USD] in the United States),[20] many cannot afford it as they earn only $75 USD per month.

Access to health care is asymmetric, with urban areas profiting from greater access to specialist cancer care, that is, secondary and tertiary centers. However, the rural sector ceiling is primary health care centers (PHCs). Although PHCs are well equipped to handle everyday illnesses, accurate diagnosis and treatment of cancer warrant tertiary center visits that are predominantly urban. This implies traveling significantly long distances. The scenario is considerably worse in Northeast India where 81.64% comprises rural

population.[21] Lack of a place to stay, long time required for investigations, limited funds, and language and cultural barriers further add to the burden.[22] Health care professionals' preferential working in urban areas has led to an unequal care capacity distribution. Government-funded hospital beds in urban areas are almost twice that of rural counterparts (0.5 *v* 0.3 million). The rapid development of the private sector in the urban setting has exacerbated such disparities.[23]

Diagnostic Disparities

Major Indian metropolitan areas are witnessing a significant concentration of diagnostic facilities for LC, whereas rural regions are ridden with limitations. For example, low-dose CT (LDCT) scans serve as initial imaging, whereas PET-CT is often used to characterize lung nodules noted during LDCT screening. Similarly, bronchoscopy and transthoracic sampling are the commonly used modalities for obtaining pathology. Although these services have remarkably grown over the past decade, their density is predominant in urban centers.[24] Transthoracic sampling is typically under image guidance (CT or ultrasound). Unfortunately, <1% of hospitals currently have an interventional radiology setup.[25]

India is a tuberculosis (TB) endemic nation where the incidence was 188 per 100,000 population in 2020 and a total of 1.9 million cases were notified in 2021.[26] Both pulmonary TB and LC exhibit comparable symptoms and radiological features including cavitary lesions, miliary patterns, and pleural effusion. Misdiagnosing these two entities is a common scenario.[27] This, coupled with a lack of awareness, precipitates a significant delay of over 3 months from the onset of symptoms to a definitive diagnosis of LC.[28] In their study from 2008 to 2018, Shu et al[29] screened 6,683 patients with TB notification in a TB-prevalent area. Forty-five (0.7%) of them, initially reported as TB, were subsequently diagnosed with LC. The COVID-19 pandemic has only made things worse by delaying the diagnosis and treatment.

Treatment Disparities

Mainstay for early-stage LC is surgical, but eventually only 1.5%-5.3% of patients undergo intervention.[30,31] Optimal decision making involves a multidisciplinary team (MDT) of medical, radiation, and surgical oncologists, radiologists, pathologists, and palliative care experts. Such MDTs are restricted to comprehensive cancer care centers and many if not all tertiary centers (Table 2). This is not the reality in rural India[33] (Fig 1).

Significant disparities in access to radiotherapy exist between rural and urban areas. Waiting times in public hospitals typically range from 1 week to 2 months versus less than a week in private hospitals. Understandably, this is a huge financial constraint for lower SES patient groups. For instance, stereotactic body radiation therapy done privately costs $700-$5,000 USD versus $10-$200 USD in the public setting.[18]

TABLE 2. Region-Wise Cancer Center Distribution and Density in India[32]

S.No	Geographical Area	Cancer Institutes
1	North	13
2	West	5
3	East	4
4	South	7
5	Central	5
6	Northeast	5

In the last decade, targeted therapy and immunotherapy have yielded significant survival benefits over conventional chemotherapy.[34] However, this requires extensive molecular diagnostic tools including next-genome sequencing, which is exclusive to tertiary care institutions, academic centers, and major private laboratories. Although first-generation targeted therapy medications like gefitinib ($175 USD per month) have been largely replaced in HICs by newer third-generation medications like osimertinib ($8,200 USD per month), they remain the mainstay in many parts of India due to cost barriers. Immunotherapy is only used first line in a very small number of patients because of limited access and high cost ($2,000-$5,000 USD). Most patients otherwise eligible for it end up with platinum-based doublet chemotherapy instead.[18] In the public sector, testing for important mutations such as the *EGFR* is limited, and newer tyrosine kinase inhibitors (TKIs) and immunotherapy medications are not available.[34]

India's representation in clinical trials amounts to only 1.5% of the total trials conducted worldwide. This disparity exacerbates itself in the Northeast region, with the highest number of cancer cases, having limited availability for participation in trials.[35] This impresses the need for improving access to clinical trials in regions with high disease densities. Fostering high-quality cancer research by the government and the private sector through clinical trials has the potential to offer accessible cutting-edge treatments.[36] However, to prevent the exploitation of vulnerable people, these must be subject to stringent governance by ethics committees.

Financial Toxicity

Indian health insurance, as touched upon earlier, consists of private and no-premium government-funded schemes.[37] Presently, there are 19 government schemes varying in sponsorship according to state.[38] Pradhan Mantri Jan Arogya Yojana is the centrally sponsored universal government scheme that is most widely used, covering 40% of the population within below poverty line.[37] In LC, it involves surgery, radiation, and systemic anticancer treatment like gefitinib and erlotinib, which has up to a maximum coverage

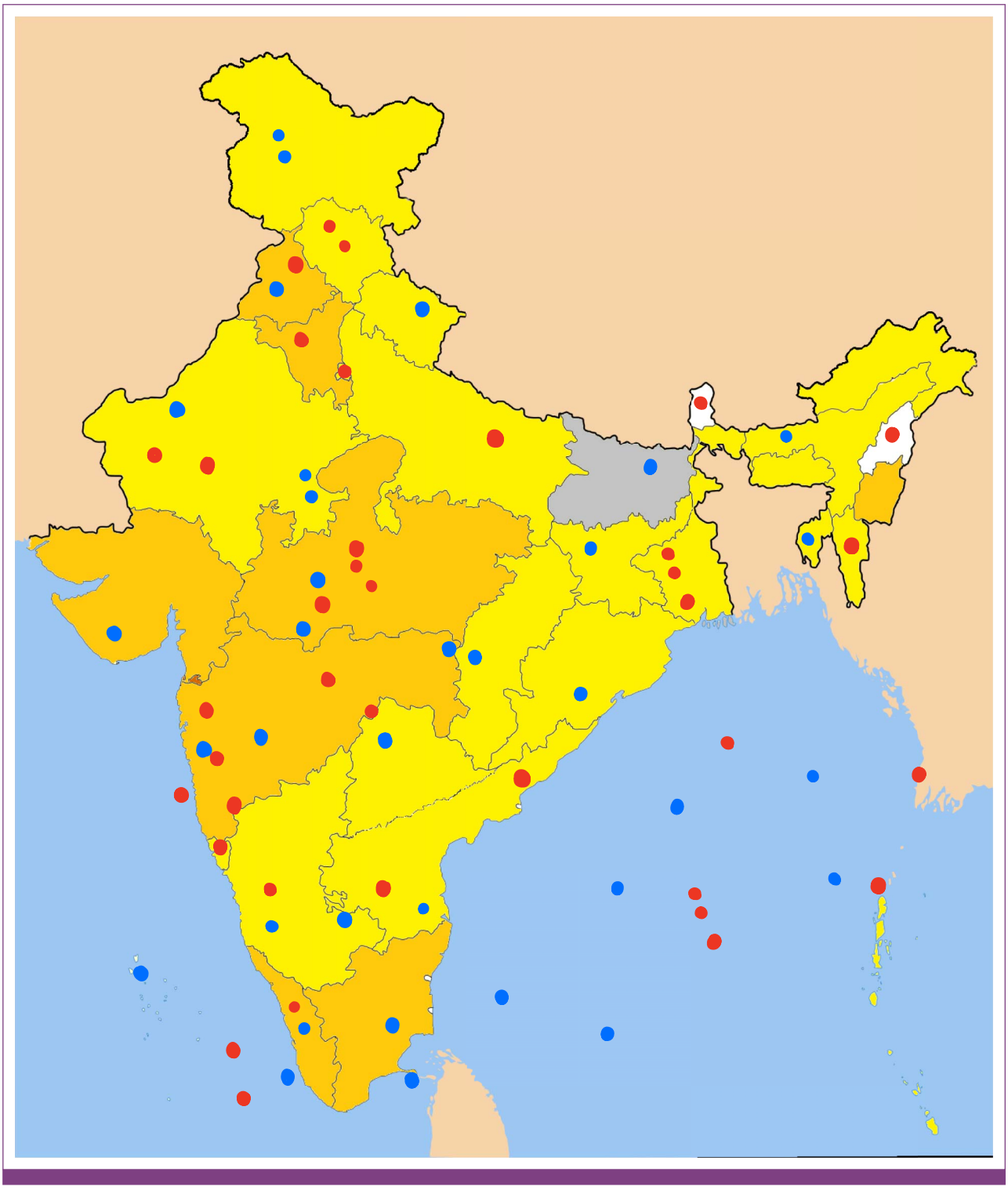

FIG 1. A visual description of the distribution of tertiary cancer centers and state cancer institutes in India.[32]

of 0.5 million Indian National Rupees (INR). Diagnostic modalities such as CT, magnetic resonance imaging, and bronchoscopy are covered, whereas testing for genetic mutations like *EGFR* is not.[39] Employer-based insurance covers a select 10% of public-funded employees by the Central Government Health Scheme and Employees' State Insurance Scheme. The 2021 data show significant disparities, that is, approximately 514 million people have insurance schemes, whereas 400 million have nil access.[38] These schemes come with a maximum coverage of 0.15-0.5 million INR which includes select diagnostic and treatment costs.[39] Private insurance has a capacity of 0.5-10 million INR.[39] However, these mostly do not involve outpatient and medication costs, leading to financial distress.

Regarding out-of-pocket expenditures (OOPE) for LC treatment specifically for those covered by government or private insurance schemes, there is no Indian study conducted till date. However, estimates vary from 0.05 to 1 million INR on the basis of the modality.[39] In the breast, cervical, and head and neck cancer setting, evidence shows significant OOPE postinsurance coverage with an average spending of 30,000-50,000 INR and pooled financial toxicity of 54%, let alone nonmedical expenses of considerable distance to travel and accommodation.[40-43]

OOPE sources of financing for cancer treatments are income (5.8%), savings (48.6%), assets (11.8%), loans (40%-66.6%), and contribution from relatives/friends (45%).[41,44] LC OOPE and financial toxicity would be expected to be worse if not equal to other primaries discussed previously. For example, TKIs and immunotherapy that are the emerging mainstay of treatment, have significant OOPE, restricting accessibility among higher socioeconomic demographics only and hence limiting availability.[45]

In conclusion, the Government of India has made efforts to create regional cancer centers in rural areas and to enhance medical institutions with oncology departments. It has pledged 1,200 million INR for the building of 20 state-level cancer centers under the National Programme for Prevention and Control of Cancer, Diabetes, Cardiovascular Disease and Stroke. The Pradhan Mantri Swasthya Yojna will see the establishment of eight new cancer facilities nationwide, as well as the gradual improvement of 58 current facilities.[46]

To summarize, LC predisposes significant morbidity and mortality in India, particularly among men, with incidence anticipated to multiply. Recent advances in diagnosis and treatment modalities have significantly improved the overall survival, although access has not been uniform. Socioeconomic and geographic variations or rather disparities are rife. There are additional challenges that are unique and regional to India, such as high population density, low literacy, delayed medical presentations, a lack of resources for molecular testing, and the unavailability of standardized therapies.[47,48]

It is critical to emphasize cancer prevention (including tobacco control), the development of cost-effective screening procedures for early detection, indigenous radiation equipment, funding generic medications, and the pursuit of drug repurposing rather than drug invention—all in the aim of building an equitable and accessible, robust, comprehensive LC program.

AFFILIATIONS

[1]Department of Medicine, Allegheny Health Network, Pittsburgh, PA
[2]Bristol Medical School, University of Bristol, Bristol, United Kingdom
[3]United Kingdom and Ireland Global Cancer Network, Manchester, United Kingdom
[4]Department of Medicine, Ascension Saint Joseph Hospital, Chicago, IL
[5]Department of Medical Oncology, Barts Cancer Centre, St Bartholomew's Hospital, Barts Health NHS Trust, London, United Kingdom
[6]Barts Cancer Institute, Cancer Research UK City of London, Queen Mary University of London, London, United Kingdom
[7]Department of Medical Oncology, Medway NHS Foundation Trust, Gillingham, United Kingdom
[8]Immuno-Oncology Clinical Network, Liverpool, United Kingdom
[9]Inequalities Network, European Cancer Organisation, Brussels, Belgium
[10]Department of Oncology, University Hospitals of Derby and Burton NHS Foundation Trust, Derby, United Kingdom
[11]Department of Medical Oncology, Tata Memorial Hospital, Homi Bhabha National Institute, Mumbai, India
[12]Department of Medical Oncology, Portsmouth Hospitals University NHS Trust, Portsmouth, United Kingdom
[13]Faculty of Science and Health, School of Pharmacy and Biomedical Sciences, University of Portsmouth, Portsmouth, United Kingdom
[14]Faculty of Medicine, Health, and Social Care, Canterbury Christ Church University, Canterbury, United Kingdom
[15]King's College London, Faculty of Life Sciences & Medicine, School of Cancer & Pharmaceutical Sciences, London, United Kingdom
[16]Kent Medway Medical School, University of Kent, Canterbury, United Kingdom
[17]AELIA Organization, 9th Km Thessaloniki - Thermi, Thessaloniki, Greece
[18]Department of Radiation Oncology, Fortis Cancer Institute, Fortis Memorial Research Institute, Gurugram, India

CORRESPONDING AUTHOR

Aruni Ghose, MBBS; e-mail: aruni.ghose1@gmail.com.

EQUAL CONTRIBUTION

M.G. R.W. and A.A. contributed equally to this work.

AUTHOR CONTRIBUTIONS

Conception and design: Rahul Winayak, Anisha Agarwal, Aruni Ghose, Kumar Prabhash, Swarupa Mitra
Administrative support: Kumar Prabhash
Collection and assembly of data: Manas Gunani, Rahul Winayak, Aruni Ghose, Rounak Das
Data analysis and interpretation: Manas Gunani, Rahul Winayak, Aruni Ghose, Vanita Noronha, Giuseppe Luigi Banna, Stergios Boussios
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Final approval of manuscript: All authors
Accountable for all aspects of the work: All authors

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Rahul Winayak
Employment: NHS

Anisha Agarwal
Employment: Ascension saint Joseph hospital

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Giuseppe Luigi Banna
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Speakers' Bureau: AstraZeneca, Astellas Pharma, Amgen, Bayer, Merck, Ipsen
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