



Setting research priorities in smokeless tobacco control: A retrospective review

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Background & objectives: Smokeless tobacco (SLT) has become a global menace; India being one of the high-burden countries contributes about 67 per cent of its users. Although research is ongoing on various aspects of SLT use and its effects, there is a need to identify the still under-researched areas in this field. This study was aimed at delineating the quantum of research on various topics of SLT, with intent to delineate research gaps for guiding future research priorities.

Methods: Data about research in SLT were collected from PubMed database using 'smokeless tobacco' as a keyword and applying Medical Subject Headings (MeSH) terms filter. Data were extracted in XML (Extensible Markup Language) format and parsed into database to extract necessary fields such as PubMed IDs, authors' names, affiliations and MeSH terms. Quantum of research in various aspects of SLT was identified for individual MeSH terms and compared for global and Indian data.

Results: Data analysis of 2857 records revealed that maximum number of articles was devoted to adverse effects (35.6%) followed by epidemiology (32.4%). In comparison, India contributed only 11.7 per cent of records with maximum number of articles on the topics of epidemiology (26%) and adverse effects (45.8%). Higher proportion of research was published on epidemiology, aetiology and prevention and control at global level, while adverse effects of SLT were researched more in Indian studies as compared to global data.

Interpretation & conclusions: The present analysis highlighted the paucity of research studies on important topics such as economics and alternative strategies of SLT control, both on the global and regional levels.

Key words Adverse effects - epidemiology - priorities - research - smokeless tobacco - trend

Smokeless tobacco (SLT) usage, initially considered a regional burden for South-East Asia, has achieved global epidemic proportions with users in 140 countries across all age groups¹. The multitude

of forms in which SLT products are available for consumption increases the complexity of research in this area. Epidemiology of SLT use across various countries has been receiving fair attention, especially

with the inclusion of questions on SLT use in the global adult tobacco survey as well as global youth tobacco survey^{2,3}.

Considering the scarcity of funds available globally for tobacco control research, there is a need to prioritize research topics likely to have an impact on vulnerable groups in the developing world. Several studies have been done to define priorities in tobacco control in general, with most of the emphases on smoking. A working group at the 10th World Conference on Tobacco or Health in Beijing suggested that research needs for prevention and cessation be found and national research complemented by subnational as well as international research⁴. Another international committee convened by the Institute of Medicine of the US Academy of Sciences, while preparing a report on cardiovascular diseases in developing countries, recommended prevalence studies, time series monitoring, cost-effectiveness of interventions to prevent smoking, and economic assessment to estimate impact of tobacco production and consumption in developing countries⁵. A report of regional meetings (Latin America, South and South-east Asia and Africa) delineated recurring themes within each regional agenda apart from specific research issues⁶. It has also been highlighted that most of the global funding for tobacco control research is utilized in health-related issues rather than multidisciplinary policy-oriented research and majority of this health effect-related research is conducted in the developed countries⁶. However, no effort has yet been undertaken to consolidate the accessible research data on SLT control and identify the specific areas still requiring attention of researchers. Although systematic reviews and meta-analysis on specific topics of SLT, for instance, adverse health effects, have been published^{7,8}, a comprehensive review of the available literature highlighting the research priorities has not been conducted. Hence, the present analysis was aimed at consolidating the available literature on SLT control in an effort to delineate the research topics in SLT that should become priority areas for researchers and funding agencies in future.

Material & Methods

Data collection and extraction: Studies conducted on SLT were retrieved from PubMed database from January 1970 to December 2016 using the keyword 'smokeless tobacco' and applying filter 'MeSH terms' (MeSH stands for Medical Subject Headings). All available articles, irrespective of the language, were included. However, filter was applied to exclude

reviews, books and commentaries, letters to editors, conference abstracts and Congress proceedings. The included articles were retrieved and stored in XML (Extensible Markup Language) format.

Further, XML parsing was performed using a scripting language, hypertext pre-processor (PHP) to extract necessary fields such as PubMed IDs, authors' names (first name, last name), title of journal, affiliations, MeSH terms and year of publication by two authors. Any disagreements between the two authors for these fields were resolved by discussion and mutual consensus. Windows, Apache, MySQL and PHP server was used for the creation of database and execution of PHP scripts. All the necessary information extracted from XML parsing was stored in the database so created. Affiliations corresponding to the first author were used to ascribe countries where SLT research was performed. The methodology adopted for this analysis is depicted in Fig. 1.

Data analysis: Subsequent to the creation of database, SQL queries were executed for retrieval of data pertaining to the fields of interest in numbers, which were then analyzed for tabulating MeSH term-wise results (global and India) and calculating year-wise trends in the research based on MeSH terms. For global data, due to large number of MeSH terms, only top 10 terms were included in the graph depicting trend.

Test of significance (Z test) between two proportions was applied to compare the global and Indian data.

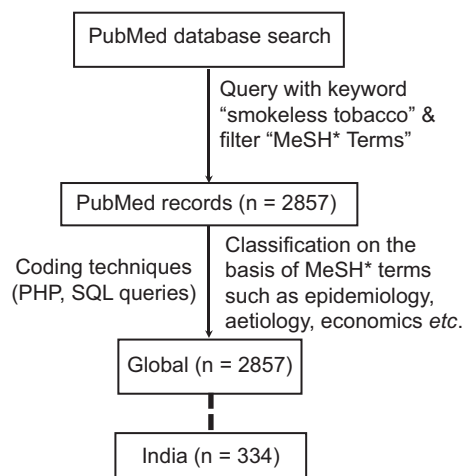


Fig. 1. Flowchart depicting methodology adopted for data analysis of PubMed records of smokeless tobacco. MeSH, Medical Subject Headings.

Results

Data of 2857 records were analyzed to identify the maximum and minimum research conducted in SLT aspects globally as well as in India. Analysis showed the trend and research gaps that varied over time from 1970 to 2016. Maximum number of articles globally was devoted to epidemiology of SLT use (32.4%) and adverse effects of these products (35.6%), as seen from the Table. Compared to the global data, India's contribution to publication in the field of SLT research was at a meagre 11.7 per cent with a total of 334 papers. In India, maximum research was devoted to adverse effects and epidemiology of SLT (Table, Fig. 2).

Global trend analysis: On a global level, SLT research showed an increasing trend since 1981 although a slight dip was noted in the period from 1991 to 1995. Research on adverse effects as well as epidemiology increased since the start of the 21st century (Figs 3, 4).

Trend analysis of publications from India: Despite the huge burden of SLT use in India, focussed research on various aspects of SLT has not been done. Data showed that the research gained some momentum in the period starting from 2000s, both in adverse effects and epidemiology (Figs 3, 4).

Comparison of global and Indian research data: Significantly higher proportion of research was devoted to epidemiology ($P<0.05$), aetiology ($P<0.01$) and prevention and control of SLT ($P<0.001$) at the global level compared to Indian data. On the other hand, significantly higher proportion of studies focussed on adverse effects of SLT were seen in Indian research compared to global data ($P<0.001$).

Discussion

The paucity of research and dearth of adequate evidence base on the extent of problem and harmful effects of SLT lead to barriers in effective implementation of SLT control measures by the interested stakeholders⁹. A recent study by Suliankatchi *et al*¹⁰ reported a shift in the preference of tobacco users from smoking to SLT use in SEAR countries including Bangladesh, India and Nepal. It has been shown that users who start with low-nicotine 'starter' products are likely to subsequently 'graduate' to products with higher-nicotine content¹¹. These facts suggest the urgent need of implementation of SLT control by all countries faced

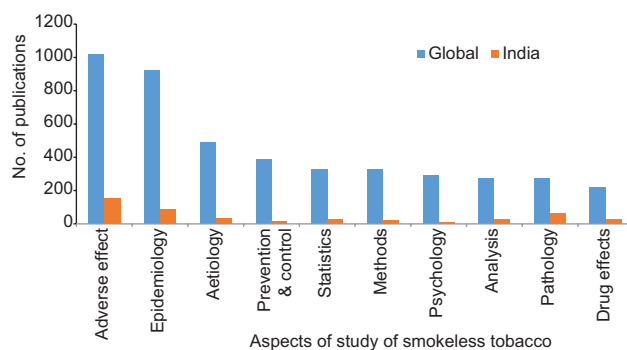


Fig. 2. Bar diagram showing research in top 10 aspects of study of smokeless tobacco from 1970 to 2016.

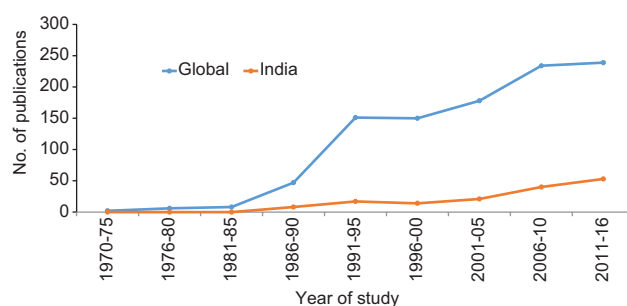


Fig. 3. Line diagram depicting the trend analysis of papers on adverse effects of smokeless tobacco (global and India) from 1970 to 2016.

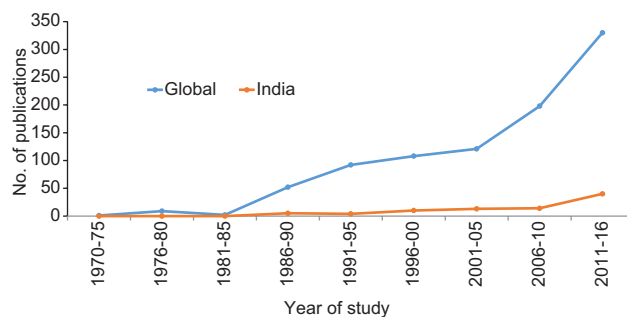


Fig. 4. Trend analysis of research on epidemiology of smokeless tobacco (global and India) from 1970 to 2016.

with the problem of rising prevalence of its use. Due to lack of consolidated data on the extent and areas of research in SLT, funding current and future research, especially in high-burden but low-income countries, is an uphill task. Hence, we attempted to consolidate the currently available research in the field of SLT and identify the research gaps and delineate topics that should be research priority for the interested stakeholders.

Our analysis demonstrated that adverse effects of SLT and epidemiological aspects have received the greatest attention of researchers. Epidemiological survey of SLT users is necessary to monitor the changing

Table. Comparison of the quantum of research articles on various aspects of smokeless tobacco - global and India data						
MeSH terms	Number of articles (%) - global	Number of articles (%) - India	MeSH terms	Number of articles (%) - global	Number of articles (%) - India	Number of articles (%) - India
Adverse effects	1017 (35.6)	153 (45.8)	Chemically induced	66 (2.3)	7 (2.1)	17 (0.6)
Epidemiology	925 (32.4)	87 (26.0)	Mortality	66 (2.3)	7 (2.1)	14 (0.5)
Aetiology	492 (17.2)	37 (11.1)	Trends	64 (2.2)	1 (0.3)	11 (0.4)
Prevention and control	389 (13.6)	15 (4.5)	Physiopathology	61 (2.1)	5 (1.5)	9 (0.3)
Statistics and numerical data	326 (11.4)	25 (7.5)	Urine	54 (1.9)	4 (1.2)	7 (0.2)
Methods	325 (11.4)	20 (6)	Economics	47 (1.6)	5 (1.5)	6 (0.2)
Psychology	290 (10.1)	9 (2.7)	Administration and dosage	44 (1.5)	1 (0.3)	6 (0.2)
Analysis	271 (9.5)	26 (7.8)	Pharmacokinetics	37 (1.3)	-	6 (0.2)
Pathology	271 (9.5)	64 (19.2)	Isolation and purification	35 (1.2)	4 (1.2)	6 (0.2)
Drug effects	218 (7.6)	26 (7.8)	Standards	33 (1.1)	1 (0.3)	5 (0.2)
Metabolism	214 (7.5)	41 (12.3)	Drug therapy	32 (1.1)	1 (0.3)	5 (0.2)
Chemistry	156 (5.5)	11 (3.3)	Ultrastructure	30 (1.0)	8 (2.4)	4 (0.1)
Toxicity	152 (5.3)	25 (7.5)	Organization and administration	29 (1.0)	-	4 (0.1)
Pharmacology	133 (4.6)	15 (4.5)	Biosynthesis	28 (0.9)	3 (0.9)	4 (0.1)
Utilization	120 (4.2)	6 (1.8)	Rehabilitation	28 (0.9)	-	4 (0.1)
Genetics	117 (4.1)	54 (16.2)	Supply and distribution	28 (0.9)	1 (0.3)	4 (0.1)
Legislation and jurisprudence	112 (3.9)	3 (0.9)	Immunology	25 (0.8)	5 (1.5)	2 (0.1)
Blood	100 (3.5)	15 (4.5)	Classification	23 (0.8)	2 (0.6)	2 (0.1)
Ethnology	98 (3.4)	2 (0.6)	Diagnosis	22 (0.8)	2 (0.6)	2 (0.1)
Therapeutic use	88 (3.1)	4 (1.2)	History	21 (0.7)	-	1 (0.04)

Contd...

MeSH terms	Number of articles (%) - global	Number of articles (%) - India	MeSH terms	Number of articles (%) - global	Number of articles (%) - India	MeSH terms	Number of articles (%) - global	Number of articles (%) - India
Therapy	82 (2.8)	8 (2.4)	Surgery	21 (0.7)	5 (1.5)	Nursing	1 (0.04)	-
Complications	81 (2.8)	-	Virology	21 (0.7)	2 (0.6)	Parasitology	1 (0.04)	-
Physiology	71 (2.5)	7 (2.1)	Microbiology	18 (0.6)	3 (0.9)	Radiation effects	1 (0.04)	-
						Transmission	1 (0.04)	-

Since individual articles could contain more than one MeSH terms, the total of numbers in Table is higher than the number of records retrieved.
*MeSH, Medical Subject Headings

prevalence as well as evolution and geographic spread of new products¹¹.

Important topics such as prevention and control of SLT, psychosocial aspects, economics and supply and distribution have not received adequate research attention till now. Evaluation of psychological issues such as factors associated with initiation of SLT use and reasons for switch from smoking to SLT products needs to be evaluated to assist the policymakers in implementing better control measures. Similarly, aspects such as economic and health costs of SLT use, including the management of its antecedent health effects, revenue estimates and gainful employment and effects of taxation policies on the consumption of SLT products, need urgent attention of researchers.

Analysis of Indian data showed the relative scant quantum of overall research on SLT with maximum focus on adverse effects and epidemiology, similar to the global data. Research related to topics such as chemistry, pharmacology, isolation and purification and microbiology was lacking from India. This fact assumes great importance considering the vast range of SLT products consumed in various parts of the country^{12,13}. Although an all-encompassing study on products available in India has not been conducted so far, a review demonstrated wide variation in the concentration of carcinogens and toxic compounds in some of Indian SLT products¹⁴. Such a variation, in turn, may lead to difference in the risk estimates of association of these products with adverse health consequences. This difference in risk estimates is liable to be utilized negatively by the tobacco industry to further their claim of SLT products as a harm-reduction measure for smokers who are not able to quit tobacco completely.

There is also a paucity of literature on economics of SLT in India. Till recently, taxation on SLT products in India was *ad valorem*, *i.e.* based on the retail price of the product¹⁵. However, an extremely low base price of the SLT products, especially relative to cigarettes, allowed the manufacturers to nullify the effects of taxation increase imposed by the government¹⁵. The recent introduction of goods and services tax (GST) on a nationwide scale in India imposed a 28 per cent GST on tobacco products and an additional cess that varied from 71 to 204 per cent (160% for *zarda* and *filter khaini*, 204% for *pan masala* with *gutka*) depending on the product¹⁶. The

impact of this new tax regimen on the consumption of SLT products is yet to be evaluated. Hence to summarize, maximum research on SLT has been focussed on adverse effects and epidemiology, with significant difference in the proportion of quantum of research between global and Indian data. Vital topics such as economics of SLT, microbiology and prevention and control are yet to receive adequate research attention.

The main strength of the analysis included the innovative design of the study and all-inclusive nature of literature search. The analysis had a few limitations that should be kept in mind while evaluating the results. Since the PubMed search was performed using only the term 'smokeless tobacco', this could have led to incomplete retrieval of papers since a few authors might have used terms of specific SLT products in their publications. However, the effect of this would, in all likelihood, have been negligible considering that the term 'smokeless tobacco' is the most frequently used phrase in such articles. The search was based on MeSH terms, and this might have led to a slight overestimation of the total number of publications. Statistical analysis revealed a difference between global and Indian research data; however, since individual articles contained multiple MeSH terms, the comparison might be somewhat erroneous.

In conclusion, the present analysis highlighted the paucity of data on important topics such as economic costs and alternative strategies for SLT control. Due to overall scarcity of research funds available, there is a need for prioritization of research topics that may be guided by the consolidated data provided by our study.

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Conflicts of Interest: None.

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