|  |  |
| --- | --- |
| **Title of the article** | Estimate of Indians suffering from Adverse Effects of Medical Treatment: A systematic analysis of all evidence during 1990-2015 |
| **Author** | Dr. Thavarajah Rooban |
| **Primary Affiliation** | Director and Consultant,  Marundeeshawara Oral Pathology Services and Analytics  B-1, Mistral Apartments, Wipro Street, Shollinganallur, Chennai-600119 |
| **Secondary Affiliation**  **[Not for Inclusion – Only Declaration]** | Professor  Department of Oral Pathology  Ragas Dental College and Hospital  2/102 East Coast Road, Uthandi, Chennai – 600 119 |
| **Mailing address** | Dr. T. Rooban  Director and Consultant,  Marundeeshawara Oral Pathology Services and Analytics  B-1, Mistral Apartments, Wipro Street, Shollinganallur, Chennai-600119 |
| **Telephone numbers** | +91-9551096200  +91-9894844721 |
| **Email ID** | [t.roobanmds@gmail.com](mailto:t.roobanmds@gmail.com) |
| **Any other authors** | Nil |
| **Declarations** | I declare no competing interests and funding support for this study |
| **Similar Work** | I have not published any related articles in the research avenue previously. However, I have submitted manuscripts based on Global Burden of Diseases Data in the past |
| **Short Title** | Study on Adverse Medical Outcomes in India |
| **File Abbreviation** | TR\_AMO |

**Estimate of Indians Suffering from Adverse Effects of Medical Treatment: A Systematic Analysis of all Evidence during 1990-2015**

**Abstract**

**Objective**: There is a paucity of data on the combined burden posed by adverse effect of medical treatment outcome (AEMTO) in India. The intend of this manuscript is to systematically review the collated data of AEMTO in terms of prevalence, death, disability-adjusted life years, years lost to disability and years lost to death and compare the data in 1990 and 2015. **Methods:** Data from Global Burden of Diseases, 2015 was searched for adverse medical treatment as per International Code of Diseases-10th Edition for all of the world and India. The study also attempted to study AEMTO in terms of age and gender in India for 2015. **Results**: The prevalence rate of AEMTO among Indians was 132 per 100,000 in 1990 and 85.02 in 2015. Globally it was 186.1 and 156.1 respectively. Age standardized rate of death for both genders combined, per 100000, with due to AEMTO was identified to be 2.54 in 1990 and 1.26 in 2015 among Indians. On considering the global death rate due to AEMTOs it was 1.88 in 1990 and 1.46 in 2015. The DALY rate per 100000 lost to AEMTO by Indians in 1990 was 105.31 and 48.1 in 2015. On comparison, on a global scale it was 115.55 and 74.1 respectively. **Discussion:** Besides discussing the strength and weakness of the results presented, the ethical and legal context of identifying AEMTOs, transparent accountability for potential harm by health care professionals, and the need for correction of root causes is underlined.

**Background:**

Health care system in India is supported by the state, central government and to a larger extent by the private sector. The extent of delivery of quality health care is the complex situation is influenced by several factors including infra-structural, personal, financial and supply contents.[1] The sheer volume of population and the fewer numbers of doctors/other para-medical personnel’s, continue to pose undue challenges. The quantity of new medical knowledge, skill and advancement generated by research community and innovations related to patient care often outpace the updating and implementation efforts of health care providers. Lack of integrated, focused continuing education programs, frequent outdating of guidelines/protocols and influencing efforts of research/pharmaceutical industry motivated by commercial gains influence the decision of health care providers.[2] In the system level, mostly, every type of hospital is often under-staffed, under-supplied, financed and equipped. Increasing burden of non-communicable diseases, frequent outbreaks of infectious diseases adds more burden on the health care providers- primarily the physicians and surgeons.[1] Because of such increasing demands, providers are often expected to give care in suboptimal situations – inclusive of working conditions, decreased/less competent or trained staff, and a shortage of manpower. In this situation, adverse outcomes are not a remote possibility. Adverse Effect of Medical Treatment Outcome (AEMTO), in its broadest definition would encompasses all unexpected and harmful experience that a Indian patient encounters as a result of being in the care of a medical professional or system because high quality care was not delivered during hospitalization. The outcome may be realized immediately, delayed for days or months, or even delayed many years.[2]

AEMTOs are often classified as errors of commission; omission; communication; context, and diagnostic errors. They are a procedural mistake or a right action but performed improperly, resulting in adverse outcomes (errors of commission), an action that was necessary as a treatment but not performed (errors of omission) or errors in communication among medical/surgical team and or patient or health care providers. Contextual errors occur when patient's unique circumstances are not taken in to consideration before instructions provided. Diagnostic errors are those arise out of improper assessment in diagnosis or in tests used to assess the disease/condition or progression.[2]

To develop focused policies to prevent AEMTOs, based on societal needs and perception, the sum total of the AEMTOs burden that Indian society faces needs to be identified. For this purpose, parameters such as prevalence, death, Disability-Adjusted Life Year (DALYs), Years Lost to Disability (YLDs) and Years Lost to Death (YLL) have been introduced and successfully used by studies such as Global Burden of Disease (GBD) studies.[3-5] The extent of AEMTOs, to the best of our knowledge is not previously reported from India. This manuscript intends to address the lacunae by projecting the combined burden posed by AEMTOs and compare the situation 25 years ago, with itself and in the global context.

**Material and Methods**

The GBD2015 study[6] included AEMTOs defined by the International Classification of Diseases, Tenth Edition as ICD- 10: Y38.9-Y84.9, Y88-Y88.3.[7,8] Age was either all ages inclusive or standardized, unless specified. Gender was not usually differentiated for the study purposes. The detailed methods are described in details elsewhere.[3-5]

Data input

The GBD2015 study includes systematic analysis from about 195 countries and territories. The prevalence of AEMTOs came from several data sources [See supplementary document]. The terms of the definitions in the GBD2015 as well as the present study are available at <http://www.healthdata.org/terms-defined>

Data Analysis

Data visualizations and collection for AEMTOs from <http://vizhub.healthdata.org/gbd-compare>. The GBD2015 is reported to utilize advanced versions of a special computer program, DisMod-MR 2.0. This program run on a series of coding programs in Python. The series of algorithm are better accessed on <http://ghdx.healthdata.org/gbd-2015-code>. This process is reported to be efficient, able to achieve stable and better internal consistency from data as supplied by the GBD2015.[9] The above designated program computes the outcome variables as prevalence of AEMTO-specific sequel—in each age group, sex, and year—times. The algorithm and the mathematical model has been described in detail elsewhere in supplementary tables.[3-5] A corresponding appropriate GBD disability weight derived from a population survey is applied.[10] This ensures that AEMTO burden is a function of public perception about AEMTO severity rather than the interpretation of the involved health care personnel.

We report total AEMTOs DALYs and rates (per 100,000 population) in addition to prevalence estimates of Indians and at a global levels in 1990 and 2015. One DALY is described as “a year of healthy life lost due to either premature mortality or disability” and the sum of DALYs as “the gap between the population’s current health status and an ideal situation where the entire population lives to an advanced age, free of disease”.[5] Uncertainty, arising from data inputs and the calculations of DALYs were subjected through a Monte Carlo simulation techniques to predict the 95% Uncertainty Interval, as previously described.[5]

The data processed in the study confirms to guidelines set by the [Guidelines for Accurate and Transparent Health Estimates Reporting (GATHER](http://gather-statement.org/), <http://gather-statement.org/>) and the metadata for the data used in the study can be accessed at the <http://ghdx.healthdata.org/gbd-2015>.

**Result:**

Globally 2897 and 266 Indian data sources and reports [See supplementary file] were identified to be associated with the AEMTOs. The number of Indians of all ages and both genders affected by AEMTO in 1990 was 1176590 while in 2015 it was 1033059. Globally it was 9417735 in 1990 and 11158614 in 2015. The prevalence rate in Indian was 132 per 100,000 in 1990 and 85.02 in 2015 while globally it was 186.1 and 156.1 respectively.

Age standardized rate of death for both genders combined, per 100000, with due to AEMTO was identified to be 2.54 in 1990 and 1.26 in 2015 among Indians. On considering the global death rate due to AEMTOs it was 1.88 in 1990 and 1.46 in 2015. The DALY rate per 100000 lost to AEMTO by Indians in 1990 was 105.31 and 48.1 in 2015. On comparison it was 115.55 and 74.1 respectively. The rate, percentage and number of YLLs and YLDs are described in Table-1. Figure 1(A and B) shows the global rate of prevalence of death and DALYs per 100000 respectively in 2015.

In India, in 2015, among both sexes, prevalence of AEMTO was seen in ≤1 years of age group after which it slowly reduced (Fig-2A). Gender wise trend difference were also observed (Fig-2B,2C). On comparing the DALYs lost, age groups showed difference in trends. Children and young adolescents had lost more DALYs than other age group. (Fig 3). The fatal AEMTO outcome and age distribution of Indians, both genders, in 1990 and 2015 are shown in Fig 4A,B while the DALYs lost to AEMTO in 1990 and 2015 between age groups are shown in Fig 5A and 5B. Global comparison of the annual percentage (1990-2015) of change of both genders, of all ages, in terms rate of death and DALYs per 100000 lost are given in Fig-6A and 6B respectively.

**Discussion**

Adverse Effect of Medical Treatment Outcomes (AEMTO) could vary from simple complications such as delayed wound healing to adverse drug reactions and even death. They are often considered synonymous with medical errors and often the near misses are not included in this spectrum.[2] The disability weight for this may range from 0.011 to 1 (death) depending on the severity of the AEMTO.

Globally the earliest, widely cited reports of AEMTO was from Institute of Medicine, USA. The report considered the outcome from 30000 selected health records. Several such record based studies quotes higher AEMTOs.[1] The present study data, emanates from population level records rather than hospital records, which is reported to have issues such as under-reporting of AEMTOs especially those AEMTOs that remain undiagnosed. Studies have revealed that AEMTOs as obtained from such records cannot be estimated in a statistically rigorous way.[1] The GBD approach may provide a robust solution as the computer program collates all known reliable data from surveys and reports applying and accounting for all variables. [See supplementary files]

In India, AEMTO monitoring is in its nascent stages and there has been only calls for building a pharmacovigilance set-up throughout the country.[11] Anecdotal evidences and media attention has been called for when AEMTOs come in focus.[12-14] To the best of our knowledge, there is no estimation of burden of AEMTOs in India and this manuscript is probably the first to predict the combined burden of AEMTO in India. Though the methodology suffers from its own set of limitations[3-5], the results offers a robust measures based on which further policies could be built. But the strength of the study emanates from the consideration of wide spectrum of reports and surveys and power of advanced computer statistical programing.

Though globally the number of AEMTO has increased during 1990 to 2015 but the prevalence rates per 100000 have reduced from 186.1 to 156.1 over the 25 year period, among Indians, though the population have increased over the 25-year period, the prevalence have reduced with the rates decreasing from 132 to 85.02. Similar trend is noted with death arising due to AEMTOs. The incidence of AEMTO as reported in GBD2013 is in line with the present report on a global level but with much more refinement in the statistical approach. On pursuing the fig-1 and 6 as well as table-1, it appears that India has been successful in reducing its combined burden of AEMTO from 1990 to 2015 in terms of prevalence, DALYs, YLLs and YLDs. It is relatively lesser than the burden faced at the global level. This could have been partially due to better pediatric care, institutionalized delivery, ante-natal and post-natal health care support system evolved since 1990.[1] The fact is exemplified in the Fig 3 to 5. The remarkable decrease in the child year group has probably influenced the outcome to a greater degree.

At the same time, the changing policies in cause of death registration has probably caused this artificial decrease in fatal AEMTOs. In 2015, it was reported that less data were available for analysis in post 2005 period, when the actual drop in AEMTOs happened in the present study.[3] Only verbal autopsy data has been released for the period of 2002-04 after which there is no or little data as seen in the data included [supplementary files]. The available data also reportedly does not confirm to internationally prescribed format rendering data input inefficient.[3-5] In addition to this important aspect, the GBD studies have inherent limitations of using poor incidence data from all registered and reliable sources. Though the newer GBD algorithm accounts for these discrepancies, the magnitude and accuracy of extrapolations needs to be factored in.[3-5] Also, the study fails to distinguish fatal from non-fatal AEMTOs as well as geographical distribution of AEMTOs in India as well as the urban and rural differences. With the GBD database to include 2016 data, shortly, hopefully all the relevant missing data would be updated soon.

The huge population of India places undue stress on the fragile health care system which is over-burdened.[1] Resultantly, the burn-out rates is high among Indian medical/surgical professionals.[15] In spite of the existing shortcomings, Indian medical professionals have been quite successful in reducing the AEMTOs, particularly in the pediatric age group in the past 25 years. As seen in Fig-1 and 6, in 2015, India ranks in low AEMTOs in par with developing nations in terms of DALYs and fatal outcome rates. However this results should be interpreted with caution as many a times AEMTOs often go unnoticed, unreported and undocumented.

Patient’s awareness of their rights is reportedly vary in India.[16.17] Ethical and legal aspects of AEMTOs are vital after securing the patient’s life and their quality of life. The need to evolve a compensatory mechanism for errors on the health care professionals is the need of the hour, which can only happen when patients are aware of their rights. All stake holders need to collude to build a system that attempts to minimize the AEMTOs, especially fatal ones and compensate for the suffering within reasonable limits as stipulated by the law of the land. The health care professionals and the nation as a whole needs to work in unison to identify and work to remove the root causes of AEMTOs. It is known that AEMTOs cannot be eliminated but can be reduced by proper procedures.

Monitoring of AEMTOs, especially on a case by case basis, would emerge crucial when the practice of existing medical system self corrects under the auspices of vigilant health care delivery monitoring system. Losing approximately 1 lakh persons owing to AEMTO reveals that India has to invest and redesign its health care, reporting and monitoring system. In India, currently, maintenance of health records rests with its citizens. A centralized health care system with electronic health record management, with consideration of ethical and safety aspects, would help to properly estimate the incidence of AEMTOs and possibly monitor the health care delivery throughout the life. The monitoring would be then dynamic rather than current static monitoring systems. Till such a system is in place, the robust values projected here in, based on the power of advanced computing, data mining and collation of all available records would help the policy framers to frame policies to minimize AEMTOs.

**CONCLUSIONS**

At global and India level, the AEMTOs are reduced in 2015 as compared to 1990. In India, The fatal AEMTOs, when happening attracts media outrage and the effects are often short-lived. The actions on such preventable, fatal and non-fatal AEMTOs are often limited. The policy makers, health providers, and public conveniently forget that they too one day may become patients and have the same risk of AEMTO.[2] In its truest sense, even by conservative estimate, lakh of people die due to AEMTOs and millions of DALYs are lost to AEMTOs is worrisome for a developing nation. In spite of this, the action and progress of building a mechanism to ensure patient safety is markedly slow. This robust estimates by a systematic review of all reliable existing data of AEMTO presented herein probably will fasten this process.

**References**

1. National Health Profile 2016. Central Bureau of Health Intelligence Publication, 2016, 1st Edition, New Delhi.
2. James TJ. A New, Evidence-based Estimate of Patient Harms Associated with Hospital Care. J Patient Saf 2013;9:122-128.
3. GBD 2013 Mortality and Causes of Death Collaborators. Global, regional, and national age–sex specific all-cause and cause-specific mortality for 240 causes of death, 1990–2013: a systematic analysis for the Global Burden of Disease Study 2013. Lancet 2015; 385: 117–71.
4. GBD 2015 Mortality and Causes of Death Collaborators. Global, regional, and national life expectancy, all-cause mortality, and cause-specific mortality for 249 causes of death, 1980–2015: a systematic analysis for the Global Burden of Disease Study 2015. The Lancet. 2016; 388:1459–1544.
5. Kassebaum NJ, Smith AGC, Bernabe E, et al., Global, Regional, and National Prevalence, Incidence, and Disability-Adjusted Life Years for Oral Conditions for 195 Countries, 1990–2015: A Systematic Analysis for the Global Burden of Diseases, Injuries, and Risk Factors. J Dent Res 2017;96:380-7.
6. From <http://ghdx.healthdata.org/gbd-results-tool>, Last accessed on 10th August 2017
7. From <http://apps.who.int/classifications/icd10/browse/2010/en#/Y40-Y84>, Last accessed on 10th August 2017
8. From <http://apps.who.int/classifications/icd10/browse/2010/en#/Y83-Y84>, Last accessed on 10th August 2017
9. Flaxman A, Murray C, Vos T, editors. Integrated meta-regression framework for descriptive epidemiology. University of Washington Press; Seattle, WA: 2014.
10. Global Burden of Disease Study 2015. Global Burden of Disease Study 2015 (GBD 2015) Disability Weights. Seattle, United States: Institute for Health Metrics and Evaluation (IHME), 2016
11. Dhikav V, Singh S, Anand KS. Adverse drug reaction monitoring in India. J Ind Acad Clinic Med 2004;5:27-33.
12. <http://timesofindia.indiatimes.com/india/Medical-errors-in-top-10-killers-WHO/articleshow/8032059.cms> Last accessed on 10th August 2017
13. <http://www.hindustantimes.com/delhi-news/careless-or-callous-the-cost-of-medical-negligence/story-EUeeGDFSySYrLfa5GKzKiI.html> Last accessed on 10th August 2017
14. <http://www.business-standard.com/article/news-ians/kolkata-hospital-asked-to-pay-compensation-for-medical-negligence-116101701330_1.html> Last accessed on 10th August 2017
15. Langade D, Modi PD, Sidhwa YF, Hishikar NA, Gharpure AS, Wankhade K et al, Burnout Syndrome AEMTOng Medical Practitioners Across India: A Questionnaire-Based Survey. Cureus 2016;8:e771
16. Unnikrishnan B, Trivedi D, Kanchan T, Rekha T, Mithra P, Kumar N et al., Patients’ Awareness About Their Rights: A Study from Coastal South India. Sci Eng Ethics 2017;23:203-14.
17. Ghooi RB, Deshpande SR. Patient rights in India: An ethical perspective. Indian J Med Ethics 2012;9:277–81.

**Figure Legends**

Fig 1A: Global rate of death due to Adverse effect of medical treatment in 2015

Fig 1B: Global rate of disability adjusted life years due to Adverse Medical Outcome in 2015

Fig 2A: Prevalence of Adverse Medical Outcome in 2015 in males in India compared by age groups

Fig 2B: Prevalence of Adverse Medical Outcome in 2015 in females in India compared by age groups

Fig 2C: Prevalence of Adverse Medical Outcome in 2015 in among both genders in India compared by age groups

Fig 3: Prevalence of Adverse effects of medical treatment in 2015 among both genders in India measured by disability adjusted life years

Fig 4A: Death among both genders due to adverse medical treatment in 1990 by age among Indians

Fig 4B: Death among both genders due to adverse medical treatment in 2015 by age among

Fig 5A: Disability adjusted life years lost due to adverse medical treatment in 1990 among Indians

Fig 5B: Disability adjusted life years lost due to adverse medical treatment in 2015 among Indians

Fig 6A: Global changes of rate of disability adjusted life years, per 100000 from 1990 to 2015

Fig 6B: Global changes of rate of death per 100000 from 1990 to 2015

Table-1: The number, percentage and rates of Disability-Adjusted Life Year (DALYs), Years Lost to Disability (YLDs) and Years Lost to Death (YLL) at India and global compared between 1990 and 2015.

|  |  |  |  |  |  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
|  |  | India | | | | | | Global | | | | | |
| 1990 | | | 2015 | | | 1990 | | | 2015 | | |
| N | 95% UI | | N | 95% UI | | N | 95% UI | | N | 95% UI | |
| Prevalence, number | All ages | 1176590 | 908257 | 1448072 | 1033059 | 807072 | 1258501 | 9417735 | 7364849 | 11480949 | 11158614 | 8773536 | 13610170 |
| Prevalence, rate | Age stand | 132 | 103 | 161 | 85.02 | 66.53 | 104.14 | 186.1 | 146.48 | 226.13 | 156.12 | 122.82 | 190.32 |
| Prevalence, Percentage | Age stand | 0.13 | 0.11 | 0.16 | 0.087 | 0.068 | 0.11 | 0.19 | 0.15 | 0.23 | 0.16 | 0.13 | 0.2 |
| Death, number | All ages | 14992 | 11241 | 19455 | 11736 | 9253 | 14836 | 102678 | 80470 | 122282 | 99755 | 77255 | 109035 |
| Death, Rate | Age stand | 2.54 | 1.97 | 3.26 | 1.26 | 0.97 | 1.57 | 2.3 | 1.88 | 2.64 | 1.46 | 1.14 | 1.6 |
| Death, Percentage | Age stand | 0.15 | 0.12 | 0.17 | 0.11 | 0.084 | 0.14 | 0.19 | 0.16 | 0.22 | 0.17 | 0.13 | 0.19 |
| DALYS, number | All ages | 931096 | 698233.76 | 1186452 | 576762 | 482207 | 712837 | 64442022 | 4605553 | 7829417 | 5384878 | 4213360 | 6360460 |
| DALYs, Rate, | Age stand | 105.30807 | 83.148282 | 131.81912 | 48.1 | 40.2 | 59.01 | 115.55 | 88.13 | 137.62 | 74.14 | 58.21 | 87.68 |
| DALYs, Percentage | Age stand | 0.16 | 0.12 | 0.2 | 0.11 | 0.092 | 0.13 | 0.24 | 0.18 | 0.28 | 0.22 | 0.17 | 0.24 |
| YLLs, number | All ages | 774254 | 1032436 | 553894 | 439049 | 352404 | 568934 | 5186671 | 3461608 | 6555720 | 3897473 | 2857947 | 4389144 |
| YLLs, Rate | Age stand | 87.71 | 65.19 | 114.21 | 36.77 | 29.46 | 46.95 | 90.74 | 65.52 | 111.83 | 53.33 | 39.23 | 59.97 |
| YLLs, percentage | Age stand | 0.16 | 0.12 | 0.21 | 0.12 | 0.094 | 0.15 | 0.24 | 0.17 | 0.3 | 0.23 | 0.17 | 0.25 |
| YLDs, number | All ages | 156842 | 97473 | 234753 | 137713 | 84876 | 206191 | 1255351 | 786860 | 1868544 | 1487405 | 926949 | 2223008 |
| YLDS, Rate | Age stand | 17.59 | 10.93 | 26.32 | 11.33 | 7.02 | 16.86 | 24.81 | 15.61 | 36.62 | 20.81 | 12.97 | 31.07 |
| YLDs, percentage | Age stand | 0.13 | 0.097 | 0.17 | 0.091 | 0.068 | 0.12 | 0.22 | 0.16 | 0.28 | 0.19 | 0.14 | 0.24 |

Rate is per 100,000 population; UI – Uncertainty Interval; Stand – Standardized; Disability-Adjusted Life Year (DALYs), Years Lost to Disability (YLDs) and Years Lost to Death (YLL)