A nationwide study of incidence and mortality due to traumatic brain injury in Ecuador (2004-2016).

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Running Tittle: Traumatic Brain Injury in Ecuador

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Abstract

Objective: Traumatic brain injury (TBI) is a global public health problem that has been underreported in developing countries. The objective of this study is to determine the incidence, mortality and geographical distribution of traumatic brain injury in Ecuador.

Methods: An epidemiological population-based analytical study of TBI in Ecuador was conducted. Hospital discharges records for men and women with a diagnosis of TBI from all age groups (0 to 110 years) were included from 2004-2016. Data was obtained from the Ministry of Public Health's national databases retrieved from the National Institute of Census and Statistics (INEC). Variables studied included sociodemographic data, overall incidence, mortality rate, case fatality rate and the risk of TBI.

Results: A total of 124,576 hospital admissions were reported, and 5,264 deaths from 2004 to 2016 due to TBI. The TBI-related hospital discharge rate was 70.68/100,000. The sex and age-specific rate for men was 90.1/100,000 and 64.1/100,000 in women. Rates were higher among Mestizos (195.6/100,000) followed by Indigenous (61.4/100,000) and Afro-Americans (14.2/100,000). The case fatality rates were higher among men over 65 years old.

Conclusion: This is the first epidemiological study of the socio-demographic distribution of traumatic brain injury in Ecuador. This study shows that young men are almost 4 times more likely to be hospitalized due to TBI than women. Fatalities due to TBI are less likely to occur among younger subpopulations, increasing significantly among the elderly. The national incidence rate decreased from 2011, suggesting that alcohol regulation might have played a role in this reduction.

Keywords: Ecuador; Traumatic Brain Injury; Epidemiology; Brain; Intracranial injury.

Background

Traumatic brain injury (TBI) is caused by any external force that might result in clinical and functional impairments in cognition(1). This type of injury has become a global health problem, affecting up to 69 million people per year worldwide(2,3). The sequelae of TBI range from mild and self-limited to chronic and potentially long-lasting disabilities(4–9). The World Health Organization estimates that motor vehicle injuries, the leading cause of injury for TBI, will be the 7th cause of mortality worldwide by 2030 (10). In spite of this, TBI has been deemed a "silent epidemic" and thought to be an underappreciated public health problem (11,12).

The global incidence of TBI is estimated to be 40 to 939 per 100,000, varying substantially between regions (2, 4 , 6 ,13–15). Recent studies in Europe revealed a crude incidence rate for all ages ranging from 47,3 to 849 per 100,000 across different countries and populations (14). The crude mortality rate ranged from 3.3 to 24.4 per 100,000 population per year, being the most common mechanisms of injury, traffic accidents and falls(14–16). The TBI hospitalization incidence rate in the US is 93.8 per 100,000 population (17). TBI incidence for Asia, region predominantly composed of low and middle-income countries (LMICs), has been noted to be 344 per 100,000 (18). Estimates of incidence for LIMC are scarce, but thought to be higher than in developed regions, which have stricter road safety regulations (8,19). The burden of TBI is also considered to be much higher in LMICs, with higher odds of death after severe TBI, higher levels of years lost to disability, and fewer resources to appropriately manage this condition throughout the lifespan (4,20,21).

Despite the geographical location, alcohol is one of the most important risk factors associated with TBI (22,23). In several studies the link between alcohol consumption, blood alcohol levels and alcohol intoxication have been associated with higher risk of TBI (23–27). Approximately 50% of the patients who had a TBI were under the influence of alcohol at the time of injury and at least 50% to 66% of all the admitted cases of TBI had alcoholaemia, yetthe rate of alcohol-screening is not higher than 50% for those reaching the hospital (27–30) The lack of these type of epidemiological data of TBI in Latin America is evident and there is a need to prioritize and coordinate funds for the generation of appropriate evidence (31,32). The aim of this study is to gather epidemiological data of TBI in Ecuador, capturing sociodemographic variables, time trends, and geographic distribution.

Methodology:

Study design and population

The present study is a country-wide population-based analysis of the epidemiology of TBI in Ecuador from 2004 to 2016. Data on discharge diagnosis of TBI, morbidity and mortality associated with TBI were obtained from the Minister of Public Health records in relationship with the number of hospital discharges from every single center accredited in Ecuador. The information is published throughout the National Institute of Census and Statistics (INEC) using International Classification of Diseases 10th Revision (ICD-10) codes for TBI (S06).

Ecuador is located in South America, bordering with Colombia to the North, Peru to the South/East and the Pacific Ocean to the west. The country is divided into 4 geographical regions: 1) the coastal region, 2) the highlands or sierra region, 3) the amazon region and 4) the insular region (Galapagos Islands). The population of Ecuador in 2016 is estimated to be 16,528,730 inhabitants based on the latest available census data from 2010 (33).

Data sources and description

All registered cases of TBI coded as S06 according to the ICD-10 were retrieved from INEC. The dataset included all the registered hospital discharges due to TBI from 2004-2016 that comes from every clinic and hospital accredited in Ecuador in a yearly basis. The ICD-10 four digit classification was also included and encompasses the following diagnosis: S06.0- Concussion, S06.1- Traumatic cerebral edema, S06.2- Diffuse traumatic brain injury, S06.3- Focal traumatic brain injury, S06.4- Epidural hemorrhage, S06.5- Traumatic subdural hemorrhage, S06.6- Traumatic subarachnoid hemorrhage, S06.8- Other specified intracranial injuries, and S06.9- Unspecified intracranial injury.

Dataset included anonymized continues and categorical data on age, sex, educational attainment, type and length of hospitalization, civil status, ethnicity, type of medical attention (private or public) and place of register (urban or rural). A combined dataset of the last 16 years of available information was created with all the cases coming from the 24 provinces and the 223 cantons (cantons are political subdivision of a province) in the country. The overall incidence, mortality, fatality rate, and relative risk were computed according to the entire population at risk by year, sex, province and canton according to the 2010 Census (33,34). The population at risk was calculated using the number of people living in that specific area during that year who would be exposed to the same risk factors as the reported cases, including information from ethnicity according to the 2010 National Census. The entire dataset is readily available as comma-separated values (CSV) or dBase database file (DBF) format in the public INEC's domain: http://www.ecuadorencifras.gob.ec/estadisticas-de-camas-y-egresos-hospitalarios-bases-de-datos/.

Ethical aspects

The analysis did not involve direct access to data of individual patients and all the information available is anonymized. According to the international good clinical and research practices and in accordance with the Ecuadorian law, ethical approval by an ethics committee and informed consent were not required.

Data analysis

The variables analyzed in the study were: sex, age, ethnicity, month, and year of the hospital admission. Information about the type of medical attention received (public vs. private); location, and the days of hospitalization were included. The incidence and mortality rates were sex and age-standardized using projection data by canton and province using the projections available at the INEC's 2010 Census (33). Incidence was calculated by dividing the number of new cases per year, by the total population at risk during each year.

The incidence and mortality rates were computed by age, sex, geographic location and their corresponding population. For age analysis, all cases were distributed in 17 age categories by every 5 years of age. General linear models (GLM) were used to assess the association of the occurrence of TBI with variables such as sex, age, ethnicity and geographical location. The appropriate GLM were chosen based on the data distribution analysis using the function "fitdist" of the "fitdistrplus" package in R(35). The proportion test with the "Bonferroni" correction for multiple comparisons was used to assess the differences in proportions of mortalilty by ethinicity.

All statistical analysis accepted significance with a p-value <0.05. Calculations were completed using the IBM Corp. Released 2014. IBM SPSS Statistics for Windows, Version 24.0. Armonk, NY: and R Core Team software 2018 version 3.5.1. Cartography was generated using QGIS Development Team 2.8.

Results:

There were 124,576 hospital admissions and 5,264 deaths due to TBI between 2004 to 2016. Men accounted for 59 % (*N* = 87,195) of the overall cases with an incidence rate of 87.1 per 100,000 while women accounted for 41 % (*N* = 37,381) representing 37.5 per 100,000.

Age and sex analysis.

The mean age was 32 (SD +/- 23 years) in men and 30 (SD+/- 27 years) in women. Relative risks and 95% confidence intervals were computed for all the age groups using women cases as the reference. The RR was significantly higher for men in every group, however, the likelihood of TBI among men 15 to 45 years old was 3.8 times higher than in women (Figure 1).

Figure 1

The presence of TBI among groups show a significant difference among men and women after adjusting for age and sex in all age groups (CI: -70.35 to -48.64 $p < 0.0001$).

Social variables

TBI is more predominant in urban areas (84% - *N* = 13,785) over rural areas (16% - *N* = 2702). The majority of cases of TBI occurred among Mestizos 91% (*N* = 21,123), Afro-Ecuadorians 1% (*N* = 154), indigenous 3% (*N* = 646), and other ethnicities 5% (*N* = 1,185). We calculated the cases by the population at risk using the total number of people in Ecuador according to the 2010 census data (33). The results show the proportions among ethnicities (Table 1).

Table 1

Incidence rates

The overall sex-specific adjusted incidence rate was 90.1/100,000 for men and 64.1/100,000 in women (Figure 2). The annual mean incidence was lower in women with 37.5 cases [36.12 - 38.99] 95% CI per 100,000 persons versus 88.3 cases [86.11 - 90.50] 95% CI per 100,000 persons in men (Table 2).

Table 2

Mortality and Case Fatality Rates

The annual mortality rate ranged from 2.11 to 3.35 per 100,000 persons at risk between 2004 to 2016. Furthermore, women had a significantly lower mortality than men in this period (Figure 3).

Figure 3

The overall distribution of TBI and the case fatality rates varied significantly by age group. For instance, younger populations (0-49 years old) accounted for more than 74.9% of the total number of cases registered, nevertheless, their mortality does not exceed 3% in average. In children younger than four, the cumulative percentage of cases reached 11.8% for boys and 20.4% for girls, nevertheless, mortality was low in both groups (1%). On the other hand, although only 25.1% of the total number of cases occurred in the patients older than 65 years old, their mortality account for more than 45% of the total number of deaths reported (Figure 3).

The association between mortality and age was assessed using a Pearson's correlation analysis. The age groups with greater proportion of TBI are correlated with lower fatality rates in men (r = -0.747 [-0.8940 to -0.4549], R^2 = 0.5581) and women (r= -0.5988 [-0.8232 to -0.2126], R^2 0.3585).

Medical Attention

The majority of patients with TBI were diagnosed and treated in the public health system (67 %; N = 83,850), followed by private for profit (31.5%; N = 39,238) and private for non-profit institutions (1.19%; N = 1,488). The average hospital length of stay (LOS) was 4 days among women and 6 in men,with a range of 1 to 1,214 days of hospitalizations. In total from 2004 to 2016, the LOS represented more than 498, 304 days.

The majority of cases of TBI were evaluated and treated in General Hospitals (42%), General Clinics (27%), Specialized Hospitals (11%), Local small hospitals (11%) and others (9%). When mortality was analyzed by type of hospital; sub-specialized hospitals (level III) have the higher mortality with 8% followed by general hospitals (level II) with 6% and basic centers and clinics (level I) with 3%. Patients admitted into general clinical wards within the hospital had a higher risk of death when compared to those admitted to a department of neurology, neurosurgery or internal medicine (*RR* = 1.27 [1.07 to 1.40], $p = 0.0028$). The months with the highest admission due to TBI were August, October and December, however, the differences among months were not statistically significant ($p > 0.05$).

Type of lesion

The majority of patients with TBI had a diagnosis of unspecified intra-cranial injury (S06.9) at admission. The worst prognosis was seen in men with intracranial injury with prolonged coma (S06.7) and among women with traumatic cerebral edema (S06.1) (Table 3).

Table 3

Geodemographic distribution

Trends by province

The provinces with the highest TBI incidence rate per 100,000 reported according to the place of residence in Ecuador are Zamora Chinchipe (122/100,000), Tungurahua (107/100,000), Pastaza (100/100,000), Cañar (100/100,000), and Azuay (97/100,000). The provinces with the highest rates of mortality are Tungurahua (4.3/100,000), Cañar (3.9/100,000), Pichincha (3.8/100,000), Azuay (3.8/100,000), and Chimborazo (3.7/100,000) (Figure 4).

Figure 4

Trends by cantons

The cantons with the highest incidence rate of TBI are Zamora (182/100,000), Azogues (156/100,000), Ambato (146/100,000), Loja (143/100,000), Santiago (141/100,000), and Cuenca (127/100,000). The mortality rate per canton showed that Limón Indanza has the highest rate of TBI (68/100,00), followed by Penipe (57 /100,00), Sucumbíos (54/100,00), San Fernando (48/100,00), Chila (41/100,00), and Chunchi (39/100,00) (Table 3 and Figure 5).

Figure 5

Discussion

This is the first study that reports epidemiological data, including geographical distribution and yearly trends of TBI in Ecuador. The incidence of TBI in Ecuador is 77.4 per 100,000, which is lower that world estimates (13). However, results are similar to data from Brazil (65.7 per 100,000), the only other country in the region with comparable data. There was an overall decrease in the incidence of TBI in Ecuador over the last 13 years (Figure 2). The incidence of TBI peaked in 2011 and then decreased significantly in the following years. The steady increase in TBI-related hospital-admissions previous 2011 might respond to several factors. One of the most likely elements associated with this trend might be the role of an increasingly high number of motorbikes entering the automotive park in Ecuador and the associated higher risk of road traffic accidents reported in the country (36).

On the other hand, the decrease seen after 2011 may be related to a national campaign that regulated alcohol consumption in Ecuador in 2010, which limited the sales and raised taxes of alcoholic beverages (37). The law prohibited the sale of alcohol after midnight on weekdays, after 2 am on Saturdays, and forbid sales of alcohol on Sundays (38). That law might have played a role limiting alcohol consumption (37,39). The impact of taxation and alcohol bans on TBI has been recently studied. In one recent publication, Posti et.al. in 2019 reported that increasing alcohol related tax of all beverage types were associated with decreased incidence rate of TBI-related death in both men and women (22). This study found that the overall alcohol consumption has decreased in similar way as the incidence rate of fatal TBI in Finland (22).

In terms of mortality, TBI related fatalities vary greatly between regions of the world, with some studies estimating 17.1 per 100,000 in USA, 11.7 per 100,000 in Europe, and 13 per

100,000 in China, although regional comparisons might be hampered by methodological variability and data availability in low middle income countries (4,40).

When adjusting for sex and age, mortality increased significantly among young and elderly men, this results are consistent with other regional studies (41). Men are at greater risk for TBI than women in Ecuador. TBI rates were higher for younger individuals, and mortality was significantly higher in individuals > 65 years old.

In Ecuador level III sub-specialty care centers receive most of the severely injured patients. This might be the reason behind higher mortality rates found in those type of hospitals (42,43). One unanticipated finding was that patients who were admitted through a non-specialized clinical ward had a 27% higher chance of dying when compared to those wards specialized in neurological care (neurology, neurosurgery or internal medicine). The possible reason of these trends might be linked to the exposure to a different standard of care like the one provided by properly trained nurses and physicians (44,45).

The higher incidence of TBI in the highland's region of Ecuador (as shown in figure 4) may be due to differences in driving conditions in mountainous regions. There is evidence of higher risk of motor vehicle accidents in mountainous vs. non- mountainous regions in other parts of the world (46). In addition, mountainous regions and irregular geographical terrain like the conditions found in the highlands and the Amazonian regions of Ecuador have also been previously associated with injury severity in motor vehicle accidents, which might lead to a higher likelihood of TBI and subsequent hospitalization (47).

TBI is more frequent in poorer provinces and in those with higher composition of Indigenous population. According to the Basic Unsatisfied Needs Database from INEC, Zamora Chinchipe, Tungurahua, and Pastaza has an average of 80%, 75% and 78.5% of people living in poverty among the rural areas, being these three provinces those with higher incidence rate of TBI per every 100,000 people (Zamora Chinchipe 121, Tungurahua 106 and Pastaza

99)(48). This relationship have been explored in Australia, where they found that the overall incidence of TBI higher among natives (166/100,000) compared to an incidence in the non-Indigenous population of (86/100,000)(49). This association probably respond to a reduced educational attainment, higher incidence of binge drinking and poorly controlled motorways among the native communities from the Amazon and the highlands of Ecuador (50–52).

The cost related to TBI in Ecuador have never been reported, nevertheless, using the National Fee-For-Services Chart and the LOS reported in our study (498,304), we estimated that at least USD $160,663,761 millions were spent in basic medical care only. These costs included one single basic visit to the ER, at least one CT-scan and the basic cost of one day of hospitalization ($300 USD per day) in a general medicine ward (53). Using data from other countries, researchers have estimated that a mild to moderate TBI can cost from $28,000 up to $120,000 USD per patient in loss of productivity, rehabilitation, medical procedures and physical and emotional sequelae (54). Extrapolating our results we can hypostatize that a minimum of 3.4 billions USD have been spent in Ecuador from 2004 to 2016 in direct and indirect TBI's costs (54–56).

Directions for Future Research

In Ecuador is urgent to explore the use of well-known policies as a mechanism to change risky behaviors throughout the subsequent years. The addition of consumption taxes, the implementation of alcohol minimum unit prices (MUP), the total or partial ban of alcohol expenditure and the reduction of alcohol related marketing are valid options that have been explored elsewhere (57–59). A further step to decrease the burden of TBI in Ecuador will be explore the link between road traffic accidents, civil violence and sport related injuries in the country.

Limitations

The main limitation of this type of analysis is the lack of individual's data concerning the cause of TBI and the presence of co-founder variables like alcohol or drug consumption. Another important fact to consider is that just clinically diagnosed TBI cases were included. Possible cases of TBI that resulted in instant deaths (like those cause by gunfire, jumping from heights or car accidents) and never reached a hospital were not available. Also, in some cases patients hospitalized for polytrauma may have a comorbid TBI that is not identified, particularly in cases of mild TBI. Additionally, TBI-related mortality data is likely underestimated, given that patients that perish without going through the hospital system were not captured in this study. Accurate diagnosis coding was not possible since the majority of cases (over 80%) were coded as unspecified brain injuries. In addition, data on TBI severity and disability after the injury is missing from the study. Lastly, in Ecuador, as in most of the Latin-American countries, there is no specialized TBI data registry and the only data available correspond to death certificates and hospital discharges as mentioned in previous reports (60). The use of nationwide secondary data could lead to information bias, particularly relevant for the validity of the cause of TBI. Finally, this work used population projections and retro-projections from, INEC's Census, which may not be an exact representation of the population growth between 2004 to 2016.

In spite of these limitations, this study represents the first systematic epidemiological effort to quantify the magnitude of TBI in Ecuador based on national health statistics. This study will provide the foundation for the implementation of evidence based public health policies to address prevention, treatment and rehabilitation programs for TBI. The development of national registry for TBI, would help gather more accurate data in Ecuador.

Conclusions

This is the first epidemiological study of the socio-demographic distribution of traumatic brain injury in Ecuador. This study shows that young men are almost 4 times more likely to be hospitalized due to TBI than women. The majority of TBI cases occurred in urban area, in the provinces within the mountainous regions and were mostly treated in public hospitals. Fatalities due to TBI are less likely to occur among younger subpopulations, increasing significantly among the elderly. The national incidence rate decreased from 2011, suggesting that alcohol regulation might have played a role in this reduction. It is important to mention that admitting patients through non-specialized clinical wards might be associated with higher mortality when compared to those patients admitted to specialized wards.

This study provides epidemiological data of TBI that will allow physicians, hospital directors, public health professionals and policy makers and others to better understand TBI and establish proper guidelines for prevention, treatment and rehabilitation of TBI in Ecuador.

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The authors have no conflicts of interest to declare.

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Authors' Contributions

Esteban Ortiz-Prado was responsible of the conceptualization and the data acquisition and analysis for the study. He drafted the main manuscript and created the figures of this work.

Guido Mascialino, Clara P. Paz and Alberto Rodriguez were responsible for the conceptualization of the manuscript. They were responsible for the elaboration of the background and discussion section.

Lenin Gómez, Katherine Simbaña and Ana Maria Diaz were fully responsible for transforming the data from XLS into CVS format. They also collaborate with the temporospectral analysis.

Marco Coral collaborate with the statistical analysis and the methodological approach.

Patricio S. Espinosa reviewed the manuscript entirely and was responsible for strengthens of the results and the discussion sections.

References

1. McKee AC, Daneshvar DH. The neuropathology of traumatic brain injury. En: Handbook of clinical neurology. Elsevier; 2015. p. 45–66.

2. Dewan MC, Rattani A, Gupta S, Baticulon RE, Hung Y-C, Punchak M, et al. Estimating the global incidence of traumatic brain injury. J Neurosurg. 2018;1-18.

3. Menon DK, Schwab K, Wright DW, Maas AI. Position statement: definition of traumatic brain injury. Arch Phys Med Rehabil. 2010;91(11):1637–1640.

4. Maas AIR, Menon DK, Adelson PD, Andelic N, Bell MJ, Belli A, et al. Traumatic brain injury: integrated approaches to improve prevention, clinical care, and research. Lancet Neurol. 2017;

5. Dikmen SS, Corrigan JD, Levin HS, MacHamer J, Stiers W, Weisskopf MG. Cognitive outcome following traumatic brain injury. Vol. 24, Journal of Head Trauma Rehabilitation. 2009. p. 430-8.

6. Te Ao B, Tobias M, Ameratunga S, McPherson K, Theadom A, Dowell A, et al. Burden of traumatic brain injury in New Zealand: Incidence, prevalence and disability-adjusted life years. Neuroepidemiology. 2015;44(4):255-61.

7. Topolovec-Vranic J, Schuler A, Gozdzik A, Somers J, Bourque P-É, Frankish CJ, et al. The high burden of traumatic brain injury and comorbidities amongst homeless adults with mental illness. J Psychiatr Res. abril de 2017;87:53-60.

8. Bryan-Hancock C, Harrison J. The global burden of traumatic brain injury: preliminary results from the Global Burden of Disease Project. Inj Prev. 1 de septiembre de 2010;16(Supplement 1):A17-A17.

9. Uski J, Lamusuo S, Teperi S, Löyttyniemi E, Tenovuo O. Mortality after traumatic brain injury and the effect of posttraumatic epilepsy. Neurology. 2018;91(9):e878–e883.

10. World Health Organization. Projections of mortality and causes of death, 2015 and 2030. Geneva; 2013.

11. Langlois JA, Rutland-Brown W, Wald MM. The epidemiology and impact of traumatic brain injury: A brief overview. Journal of Head Trauma Rehabilitation. 2006.

12. Wilson MH. Traumatic brain injury: an underappreciated public health issue. The Lancet Public Health. 2016.

13. Nguyen R, Fiest KM, McChesney J, Kwon CS, Jette N, Frolkis AD, et al. The international incidence of traumatic brain injury: A systematic review and meta-analysis. Vol. 43, Canadian Journal of Neurological Sciences. 2016. p. 774-85.

14. Brazinova A, Rehorcikova V, Taylor MS, Buckova V, Majdan M, Psota M, et al. Epidemiology of Traumatic Brain Injury in Europe: A Living Systematic Review. J Neurotrauma. 25 de agosto de 2016;neu.2015.4126.

15. Peeters W, van den Brande R, Polinder S, Brazinova A, Steyerberg EW, Lingsma HF, et al. Epidemiology of traumatic brain injury in Europe. Acta Neurochir (Wien). 14 de octubre de 2015;157(10):1683-96.

16. Majdan M, Plancikova D, Brazinova A, Rusnak M, Nieboer D, Feigin V, et al. Epidemiology of traumatic brain injuries in Europe: a cross-sectional analysis. Lancet Public Health. diciembre de 2016;1(2):e76-83.

17. Faul M, Coronado V. Chapter 1 - Epidemiology of traumatic brain injury. En: Traumatic Brain Injury, Part I. 2015. p. 3-13.

18. Tagliaferri F, Compagnone C, Korsic M, Servadei F, Kraus J. A systematic review of brain injury epidemiology in Europe. Vol. 148, Acta Neurochirurgica. 2006. p. 255-67.

19. Andelic N. The epidemiology of traumatic brain injury. Lancet Neurol. 2013;12(1):28–29.

20. Hyder AA, Wunderlich CA, Puvanachandra P, Gururaj G, Kobusingye OC. The impact of traumatic brain injuries: A global perspective. NeuroRehabilitation. 2007;22:341-53.

21. de Silva MJ, Roberts I, Perel P, Edwards P, Kenward MG, Fernandes J, et al. Patient outcome after traumatic brain injury in high-, middle- and low-income countries: Analysis of data on 8927 patients in 46 countries. Int J Epidemiol. 1 de abril de 2009;38(2):452-8.

22. Jussi P. Posti, Matti Sankinen, Jussi O. T. Sipilä, Jori O. Ruuskanen, Jaakko Rinne, Päivi Rautava, et al. Fatal traumatic brain injuries during 13 years of successive alcohol tax increases in Finland – a nationwide population-based registry study. Sci Rep. 2019;(1):1.

23. Albrecht JS(1), Smith GS(1 4), Afshar M(2), Stein DM(3). Association of Alcohol with Mortality after Traumatic Brain Injury. Am J Epidemiol. 01 de 2018;187(2):233-41.

24. Cheever CS(1), Barbosa-Leiker C(2). Impact of Alcohol Screening for Traumatic Brain Injury Patients Being Admitted to Neurosurgical Intensive Care Unit. J Neurosci Nurs. 01 de 2018;50(2):83-7.

25. Bjarkø VV(1), Helseth E(1 8), Skandsen T(2 4), Moen KG(2 7), Gulati S(2 5), Vik A(2 5), et al. Time of Injury and Relation to Alcohol Intoxication in Moderate-to-Severe Traumatic Brain Injury: A Decade-Long Prospective Study. World Neurosurg. 01 de 2019;122:e684-9.

26. Mathias JL, Osborn AJ. Impact of day-of-injury alcohol consumption on outcomes after traumatic brain injury: A meta-analysis. Neuropsychol Rehabil. 18 de 2018;28(6):997-1018.

27. MacLeod JB, Hungerford DW. Alcohol-related injury visits: do we know the true prevalence in US trauma centres? Injury. 2011;42(9):922–926.

28. Salim A, Ley EJ, Cryer HG, Margulies DR, Ramicone E, Tillou A. Positive serum ethanol level and mortality in moderate to severe traumatic brain injury. Arch Surg. 2009;144(9):865–871.

29. Lange RT, Iverson GL, Franzen MD. Short-term neuropsychological outcome following uncomplicated mild TBI: Effects of day-of-injury intoxication and pre-injury alcohol abuse. Neuropsychology. 2007;21(5):590.

30. Taylor CA, Bell JM, Breiding MJ, Xu L. Traumatic brain injury–related emergency department visits, hospitalizations, and deaths—United States, 2007 and 2013. MMWR Surveill Summ. 2017;66(9):1.

31. Puvanachandra P, Hyder A. Traumatic brain injury in Latin America and the Caribbean : a call for research. Salud Pública México. 2008;50(1):13-5.

32. Hyder AA, Wunderlich CA, Puvanachandra P, Gururaj G, Kobusingye OC. The impact of traumatic brain injuries: a global perspective. NeuroRehabilitation. 2007;22(5):341-53.

33. INEC. Censo de Población y Vivienda. 2010.

34. INEC. Estadística de Camas y Egresos Hospitalarios. 2017.

35. Team RC. R Foundation for Statistical Computing; Vienna, Austria: 2014. R Lang Environ Stat Comput. 2018;2013.

36. Algora-Buenafé AF, Suasnavas-Bermúdez PR, Merino-Salazar P, Gómez-García AR. Epidemiological study of fatal road traffic accidents in Ecuador. Australas Med J Online. 2017;10(3):238.

37. SRI. Ley Orgánica para el Equilibrio de las. Finanzas Públicas. 2016.

38. Ministerio del Interior. Regulación de venta de bebidas alcoholicas. Acuerdo Ministerial 1470 [Internet]. 2010. Disponible en: https://www.turismo.gob.ec/wp-content/uploads/2016/04/ACUERDO-1470-EXPENDIO-DE-BEBIDAS-ALCOHOLICAS-EN-ESTABLECIMIENTOS-TURISTICOS-Y-NO-TURISTICOS.pdf

39. Turismo M de. Regulación de Ventas de Bebidas Alcohólicas. Ecuador; 2010.

40. Cheng P, Yin P, Ning P, Wang L, Cheng X, Liu Y, et al. Trends in traumatic brain injury mortality in China, 2006–2013: A population-based longitudinal study. PLoS Med. 2017;14(7).

41. de Almeida CER, de Sousa Filho JL, Dourado JC, Gontijo PAM, Dellaretti MA, Costa BS. Traumatic brain injury epidemiology in Brazil. World Neurosurg. 2016;87:540–547.

42. Sampalis JS, Denis R, Frechette P, Brown R, Fleiszer D, Mulder D. Direct transport to tertiary trauma centers versus transfer from lower level facilities: impact on mortality and morbidity among patients with major trauma. J Trauma Acute Care Surg. 1997;43(2):288–296.

43. Ghajar J, Hariri RJ, Narayan RK, Iacono LA, Firlik K, Patterson RH. Survey of critical care management of comatose, head-injured patients in the United States. Crit Care Med. 1995;23(3):560–567.

44. McGloin H, Adam SK, Singer M. Unexpected deaths and referrals to intensive care of patients on general wards. Are some cases potentially avoidable? J R Coll Physicians Lond. 1999;33(3):255–259.

45. Dudley RA, Johansen KL, Brand R, Rennie DJ, Milstein A. Selective referral to high-volume hospitals: estimating potentially avoidable deaths. Jama. 2000;283(9):1159–1166.

46. Rusli R, Haque MdM, King MJ, Wong SV. A comparison of road traffic crashes along mountainous and non-mountainous roads in Sabah, Malaysia. Cent Accid Res Road Saf - Qld CARRS-Q. 30 de agosto de 2015;

47. Liu G, Chen S, Zeng Z, Cui H, Fang Y, Gu D, et al. Risk factors for extremely serious road accidents: Results from national Road Accident Statistical Annual Report of China. PLoS ONE. 2018;13(8):e0201587.

48. INEC. Pobreza por Necesidades Básicas Insatisfechas [Internet]. Insituto Ecuatoriano de Estadisticas y Censos; 2018. Disponible en: http://www.ecuadorencifras.gob.ec/pobreza-por-necesidades-basicas-insatisfechas/

49. Esterman A, Thompson F, Fitts M, Gilroy J, Fleming J, Maruff P, et al. Incidence of emergency department presentations for traumatic brain injury in Indigenous and non-Indigenous residents aged 15–64 over the 9-year period 2007–2015 in North Queensland, Australia. Inj Epidemiol. 2018;5(1):40.

50. Bombardier CH, Rimmele CT, Zintel H. The magnitude and correlates of alcohol and drug use before traumatic brain injury. Arch Phys Med Rehabil. 2002;83(12):1765–1773.

51. Rutland-Brown W, Wallace LD, Faul MD, Langlois JA. Traumatic brain injury hospitalizations among american indians/alaska natives. J Head Trauma Rehabil. 2005;20(3):205–214.

52. Kelley MJ. “Native Americans, Neurofeedback, and Substance Abuse Theory”. Three Year Outcome of Alpha/theta Neurofeedback Training in the Treatment of Problem Drinking among Dine’(Navajo) People. J Neurother. 1997;2(3):24–60.

53. Presidencia del Ecuador. Tarifario de prestaciones para el sistema nacional de salud. 2014.

54. Humphreys I, Wood RL, Phillips CJ, Macey S. The costs of traumatic brain injury: a literature review. Clin Outcomes Res CEOR. 2013;5:281.

55. McGregor K, Pentland B. Head injury rehabilitation in the UK: an economic perspective. Soc Sci Med. 1997;45(2):295–303.

56. Ashley MJ, Schultz JD, Bryan VL, Krych DK, Hayes DR. Justification of post-traumatic brain injury rehabilitation using net present value techniques: a case study. J Rehabil Outcomes Meas. 1997;1(5):33–41.

57. Holmes AH, Moore LS, Sundsfjord A, Steinbakk M, Regmi S, Karkey A, et al. Understanding the mechanisms and drivers of antimicrobial resistance. The Lancet. 2016;387(10014):176–187.

58. Lonsdale AJ, Hardcastle SJ, Hagger MS. A minimum price per unit of alcohol: A focus group study to investigate public opinion concerning UK government proposals to introduce new price controls to curb alcohol consumption. BMC Public Health. 2012;12(1):1023.

59. Pechey R, Burge P, Mentzakis E, Suhrcke M, Marteau TM. Public acceptability of population-level interventions to reduce alcohol consumption: a discrete choice experiment. Soc Sci Med. 2014;113:104–109.

60. Ortiz-Prado E, Simbaña K, Gómez L, Henriquez-Trujillo AR, Cornejo-Leon F, Vasconez E, et al. The disease burden of suicide in Ecuador, a 15 years' geodemographic cross-sectional study (2001–2015). BMC Psychiatry. 2017;17(1):342.

Figure Legends:

Figure 1 Relative Risk of TBI among age groups. Females were used as a reference group.

Figure 2 Traumatic Brain Injury 2004-2016 by gender.

Figure 3 Case fatality rate (%) among age groups versus the number of cases per group from 2004-2016. Men are represented with black filled circles and women in empty circles.

Figure 4 TBI Incidence rate /100,000 by province from 2004-2016

Figure 5 TBI Incidence rate /100,000 by canton from 2004-2016