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THE EPIDEMIOLOGY OF STROKE IN A DEVELOPING COUNTRY (PAKISTAN)

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ABSTRACT

Ischemic stroke is a major cause of neurological morbidity and mortality. The objective of this review article is to summarize facts pertaining to acute ischemic stroke and its various aspects in a developing country like Pakistan, where resources are limited and the healthcare system is underdeveloped. No large-scale epidemiological studies are available to determine the true incidence of stroke in Pakistan. We conducted a study to determine the prevalence of several important stroke risk factors among Pakistani stroke patients, and to determine whether these risk factors differ among urban versus rural populations. We also used existing data from literature to compare overall stroke incidence in Pakistan to that in developed countries. In this study we found that for stroke besides hypertension, prolonged contraceptive use and pregnancy are additional risk factors in Pakistan. Which is more prevalent in urban populations than rural population? Developed countries except Germany have much lower stroke incidences than Pakistan.

KEYWORDS: Stroke, Pakistan, Developing Countries, Epidemiology, Risk Factors

INTRODUCTION: Epidemiologic studies on stroke help us to understand the natural history of the disease and to make out risks and prognostic factors that can lead to better knowledge of the markers for disease mechanisms [1, 2]. Epidemiological and observational data can inform scientists of possible unique areas for more focused research. Both could help identify the individuals, groups, or geographic areas that are at increased risk of disease or poorer prognosis. Study of predisposing factors for stroke can lead to a better understanding of the underlying causes. In addition, knowing which individuals, communities, or regions are at risk of stroke could help physicians and public health policymakers to build up more proficient, purposeful programs to the recently published literature, at present Pakistan has an enormous proportion of its population suffering either from diabetes or hypertension or both [11, 12]. Unfortunately, a greater part of people are unaware of their comorbid conditions. This principally is due to a lack of awareness for routine medical checkup, none availability of screening services for endemic diseases locally, and unawareness on the part of the community regarding

personal healthcare [13, 14]. Even those who have been timely diagnosed mostly do not follow the standard practice of a regular follow up and/or compliance with medication [15, 16].

The current incidence and prevalence of stroke in Pakistan is not exactly known. Several reported case series in literature highlighting significant differences in terms of stroke epidemiology and risk factors for stroke subtypes. However, actual data are still not available [17, 18]. Regarding Pakistan, the current published literature is insufficient, and original research articles are not more than a few in number. Pakistan has the world's highest rate of stroke per capita, so it would be highly beneficial to collect and interpret local epidemiological data [19, 20]. A timely and appropriate management of stroke can help in minimizing morbidity/mortality of stroke and the tremendous health care cost.

The aim of this article is to clarify the important risk factors of stroke in Pakistan. Through this study, we primarily aim to present the current epidemiological stroke risk factor data in Pakistan, as well as to compare stroke incidence in Pakistan with that of the

developed world. We also intend to highlight areas for future development and improvement in management. In China, in a survey population of nearly 480687 individuals, a significant numbers are (7672) diagnosed as stroke prevalence (1596/100000) individuals and 1643 as stroke incidence (345.1/100000) individuals per year [21, 22]. In this study population, the pathological variant of stroke as diagnosed by computed tomography and brain CT scan were 90% prevalence while 83% incident stroke cases respectively. [23, 24]. In men aged ≥ 45 years; the age-specific stroke prevalence was significantly greater than in women ($p < 0.001$). In China, the most important preventable risk factors are high blood pressure, alcohol abuse, and smoking. As of today, for stroke, the most important preventable risk factor is hypertension [25, 26]. As of 2013, the stroke prevalence estimates were statistically greater than those documented in China 30 years earlier, in particular amongst rural inhabitants [27, 28].

In Pakistan, the indigenous epidemiological data are sparse. The current incidence and prevalence of stroke is not exactly known. Several reported case series in literature highlighting significant differences in terms of stroke epidemiology, risk factors, and stroke subtypes have been published [29,30]. For a better understanding of the cause and effect risk factors, it is imperative to work on the information connected to the indigenous population.

The purpose of this study was to expand on epidemiological stroke data for Pakistan by answering the following research questions:

1. What are the percentages of incidence of risk factors in Pakistani stroke patients?
2. Are there differences in the percentage patients with risk factors between urban and rural stroke patients?
3. Is there a difference between Pakistani incidence of stroke and developed nations?

We used a combination of primary and historical data drawn from literature to answer the research questions. After presenting a literature review on stroke management in Pakistan, we present the methodology of the study, followed by our results and conclusions.

2. LITERATURE REVIEW

The objective of this review is to highlight the health care and economic limitations of management of stroke in Pakistan, where there is still research work to be done, and where there are scarce resources for handling the real health problem of stroke. We reviewed and compared current research from other countries to the epidemiological data of Pakistan. This is important

to clarify the gap in knowledge and limitations faced in the management of stroke.

2.1 DEFINITIONS AND DIAGNOSIS

Stroke, or CVA, is a well-known condition causing a substantial communal burden including disability, neurological morbidity, and mortality. The diagnosis of stroke depends upon clinical observations. According to the World Health Organization, stroke is defined by “rapidly developing clinical signs of focal disorder of cerebral function, with symptoms enduring 24 hours or over and could lead to death, with no obvious cause other than of vascular origin”[31,32]. Standards for classification of stroke subtypes have not been fully understood and may swing from one study to another. As a consequence, epidemiological studies may underestimate the total burden of cerebrovascular disease.

Distinction between ischemic and hemorrhagic infarction can only be obtained by computed tomogram (CT) immediately after the incidence of stroke or at autopsy. Clinical and diagnostic test criteria make subarachnoid hemorrhage a distinct epidemiological entity because, in most cases, these patients are admitted to hospital or die before medical attention can be sought. Therefore, it is imperative to make out the subarachnoid hemorrhage as a distinctive epidemiological entity before these cases become more serious and seek medical treatment.

Transient ischemic attack (TIA), or “ministroke”, is a subtype of stroke with recent difficulty in definition. Originally, TIA was defined based on the duration of the event. An expert group recently suggested a formal change in the definition of TIA to a “transient episode of neurological dysfunction caused by focal brain, spinal cord, or retinal ischemia, without acute infarction,” thereby abolishing the time based component documented in the classical definition [33, 34]. The conclusion to use a tissue based (not an arbitrary time based) definition of TIA was primarily driven by modern imaging data, which discovered that as many as 50% of patients with momentary deficits lasting < 24 hours have evidence of brain ischemia on initial magnetic resonance imaging (MRI), and 50% of those with initial abnormalities on MRI showed substantiation of fixed infarction on following images [35, 36].

2.2 PREVALENCE AND INCIDENCE

The global impact of stroke seems to be even more pronounced than it is in the United States, but estimates of the disease burden in developing countries vary widely[37,38]. In most industrialized

populations, stroke is the third most important cause of death, hospital admission, and long-term disability. Our study took place in the developing country of Pakistan. In Pakistan, there was a crude age and sex adjusted stroke incidence of 95 per 100,000 persons per year for the following Years 2000 to 2016, with the highest incidence being 584,000 of 650,000, noted among individuals aged 75 to 85[39, 40]. Other population-based TIA incidence rates average 25 per 100,000 persons per year from 2014-2016[41, 42]. The risk of possible vascular events within 3 months is elevated after TIA, as after stroke, and this risk is uppermost within the first week after TIA [43, 44]. According to recent studies, there is 10%- 20% risk of stroke for a 90-day period after TIA. Based on this finding, prediction scores have been developed and validated to facilitate better decision making in the evaluation of imminent risk of stroke after TIA [45, 46]. Similar scores could potentially be engaged to identify TIA patients who may need admission, but have not yet been tested clinically. In ongoing epidemiological studies, cerebral ischemia noticed on brain imaging among asymptomatic persons aged 50 to 64 years is 12%, and for those individuals aged ≥ 70 years is 43% [47, 48].

2.3 RISK FACTORS

In order to reduce the burden of stroke, prevention still remains the best therapeutic at the global level. There are several published studies on stroke risk factors in Pakistan [49,50]. One follow up study helped in the identification of two groups of risk factors: Preventable and non preventable risk factors. The latter is associated with high stroke risk [51, 52], whereas the former is associated with relatively lower risk of stroke. Preventable risk factors are open to intervention for lower stroke risk; these include diabetes mellitus, cardiovascular causes such as high blood pressure, raised cholesterol, smoking, valvular heart diseases, obesity/ hyperlipidemia, sedentary habits, diet high in fats and carbohydrates, neuropsychiatric disorders, and postoperative conditions.

PREVENTABLE HEALTH RISK FACTORS. High bloodpressure (hypertension) is the most well-known malleable risk factor for ischemic stroke, and it affects over 75 million adult's ≥ 20 years of age in the United States [53, 54]. Because of its high prevalence, the population-based risk of hypertension for stroke is approximately 40% [55, 56]; while in some studies the population-based risk has been even higher, at 50%–60% [57, 58]. The prevalence of hypertension is directly related to lifestyle and the degree of mental stress and strain. In the current study, most of the

patients with cerebrovascular stroke had high blood pressure [59, 60].Cardiac arrhythmia or chronic atrial fibrillation (AF) is also a strong stroke risk factor and is apt to engage over 2.6 million individuals in the United States, according to 2010 data [61, 62]. The prevalence of AF in individuals 30–65 years of age is about 6% [63, 64]. Ever since the prevalence of AF rises with age, the causative risk of stroke due to AF is greatest in older age groups[65,66]. So, for instance, AF may account for as much as 20%–25% of strokes in individuals aged 30 to 90 years [67, 68]. The risk is about 20 times higher in those with valvular heart diseases (in particular rheumatic heart diseases) and nearly 6 times greater in those with non-valvular heart diseases [69, 70]. Clinical trial and epidemiological data have been employed to derive various stroke risk stratification schemes that can be used in clinical practice for AF patients [71, 72]. Of note, outpatient incessant arrhythmia monitoring is increasingly showing that AF may actually be responsible for a higher percentage of unexplained strokes than was previously known.

Individuals with coronary artery disease have two time higher risk of stroke compared with patients without coronary artery disease. Patients with coronary artery disease with left ventricular hypertrophy have nearly three times the risk of stroke, while those with coronary artery disease and congestive heart failure have about a fourfold higher risk of developing stroke [73, 74]. In patients with old myocardial infarction of about five years and higher, the rate of stroke is 8.1%; also, those with ejection fraction of less than 28% have relatively much higher risk of stroke [75, 76].

In a follow up study, diabetes individuals had nearly 23% higher risk of developing ischemic stroke. The incidence was about 20% higher among those with advancing age. Moreover, patients with higher levels of insulin resistance were more likely to have a first ischemic stroke [77, 78].

The metabolic syndrome (obesity, glucose dysmetabolism, hypertension, and Hyperlipidemia) has been shown to bestow a greater risk of first and recurrent stroke [79, 80].

It is unclear whether metabolic syndrome is associated with a greater risk of first stroke than what one would expect for its components [81, 82].

Finally, asymptomatic carotid stenosis with surge as a potential cause of ischemic stroke rises with age. This can be important to consider in those > 50 and is found in nearly 60% of stroke patients [83, 84]. Current medical treatment has led to much better prognostic Outcomes, with the effect that the risk of stroke associated with asymptomatic carotid stenosis have fallen significantly during the past 20 years [85, 86].

Preventable life style risk factors. Smoking is associated with lesser blood vessel elasticity, high fibrinogen levels, an increased platelet aggregation, higher haematocrit, and high density lipoprotein cholesterol levels [87, 88]. Depending upon the dose response relationship, for smokers the relative risk of stroke compared with statistics from earlier studies was near to twofold, and a dose response association with higher stroke risk has been observed in heavy versus light smokers [89, 90].

Stroke risk dwindles with smoking cessation for five years. Even passive cigarette smoking boosts progression of atherosclerosis and entails a greater risk of stroke. Further, smoking facilitates the action of oral contraceptives, enhancing the risk of stroke by several folds [91, 92].

Increased physical activity is linked with lowering of fibrinogen, homocysteine, and platelet activity. It is also associated with elevation of high density lipoproteins and increased plasminogen activator activity. Therefore, increased physical activity is associated with much lower risk of stroke, whereas sedentary behavior is associated with higher stroke risk [93, 94].

High stroke risk has been connected with all stages of hypertension and isolated systolic hypertension [95, 96]. In fact, the risk of stroke seems to have a incessant association with blood pressure down to levels as low as 115/75 mmHg [97, 98]. In light of this, the national guidelines redefined categories of hypertension so that normal systolic blood pressure is < 120 mmHg and normal diastolic blood pressure is < 80 mmHg [99, 100]. Most recently, it has been suggested that variability in blood pressure measurements (visit to visit, distinct measurements within a given visit) are associated with greater risk of stroke [101,102].

2.4 STROKE OUTCOMES

The overall death rates from stroke in industrialized countries among people over age 65 years is about 10%–12%, and nearly 88% of the deaths ascribed to stroke are among people over 65 years [103,104]. In recent decades, in most industrialized nations, an average annual decline of about 7% has been documented since 1970.[105,106]. Death rates from stroke have fallen dramatically in Japan and the United States [107,108]. Nevertheless, stroke is still the fourth most important cause of death in the United States and the main cause of enduring disability worldwide [109,110]. It is likely that, in the United States, someone dies of stroke every four minutes. By contrast, with changing risk factors for stroke, death rates have increased over the past two decades in

some eastern European countries such as the Czech Republic, Hungary, and Bulgaria [111,112]

EFFECT OF AGE ON OUTCOMES.

The incidence of stroke has direct association with age, and in hospital mortality and case fatality also increase with advancing age [113,114]. People ≥ 80 years old with stroke had a longer length of stay in contrast to younger patients (24.7 ± 27.6 vs. 22.3 ± 24.2 days; $p = 0.013$) [115,116]. Furthermore, case fatality rate for the same age group can be as high as 21% [117,118]. Although age seems to influence activities of daily living recovery; it has not been found to have an outcome on neurological recovery. This fact may advocate that older patients have a poorer capability to recover, and therefore may benefit from rehabilitation with a focal point on activities of daily living [119,120].

EFFECT OF GENDER ON OUTCOMES.

There is inadequate data recognizing gender as a cause of mortality from stroke. Due to their permanence, the overall age adjusted stroke mortality rates for men are more than for women, yet every year more women die of stroke than men. Women accounted for nearly 61% of all stroke deaths in the United States in 2015 and 2016[121,122]. This is because women have more severe strokes than men. In the ongoing study, case fatality for men was 20.2% and for women it was 25.5%; therefore, it is about 1.26 times higher among women [123,124]. Furthermore, women who survive stroke appear to have fewer encouraging outcomes than men. Health care facility stays among women are comparatively longer [124,125]. Women have relatively less favorable prognoses and worse self care at 3 to 6 months post stroke, even after adjustment for age, comorbidities, and other clinical features. It is unclear why these gender differences exist [126, 127].

EFFECT OF SOCIOECONOMIC STATUS ON OUTCOMES

The association between poverty and health disparity has been established in many different countries and at Different levels of national healthcare Coverage [128,129]. What drives this relationship is unclear, because comparisons between published studies are difficult to make due to the heterogeneity of the studies, including the choice of which indicator of socioeconomic status (SES) to measure (income, education, occupation, class, and so forth). The fact remains that these proxy measures of SES have been shown to be inversely linked with stroke case fatality, poorer

functional and motor recovery during rehabilitation, less health services after stroke, and increased recurrent stroke risk [130,131].

Stroke burden and mortality vary greatly geo-geographically, but low income countries are the most affected. Some possible mechanisms by which SES variables are associated with disease outcomes are by creating differentials in the use of social support structures, healthcare

Non communicable diseases like stroke are the leading killers in low and middle income countries like Pakistan [132,133]. A cross sectional survey from a multi ethnic transitional Pakistani community confirmed that almost a quarter of the respondents had suffered a cerebrovascular event (either a stroke or a TIA) [134,135]. Thus, there is a need to generate regionally specific data from these regions to devise effective management strategies for stroke survivor.

There are studies done in developed countries investigating the functional and cognitive outcomes of stroke [136,137]. Data from Pakistan are restricted to a few hospital based studies that have reported mortality and acute complications [138,139]. However nothing is known of the post hospital outcomes of stroke survivor. There are reasons to suspect that outcomes from stroke in developing countries akin to Pakistan may be sufficiently different from the developed world to merit investigation. Stroke etiology is different, intracranial disease being more common, intracranial hemorrhage (ICH) constitutes a higher proportion of strokes; patients are younger and ethnically divergent. A recent study has highlighted this regional difference in stroke outcomes and mortality reported in various stroke trials [140,141].

In developing countries like Pakistan, stroke is the leading cause of death and disability. Incidence of stroke is acknowledged more in urban areas than rural region of this country [142,143]. The noticeable cause is regular travel automobiles, sedentary habits, and relative fretfulness and trepidation. The urban to rural incidence ratio is 3:2. It is relatively more in well of than poor working class of communities because of sedentary habits and easier lives compared with the working class [144,145]. The incidence rate of stroke is more in cold climates like northern areas, the high Altitudes mountainous belt extending from Pakistan, boarder regions of China, Afghanistan, and Iran [146,147].



Figure1 . Map showing frequent and less frequent flow of patients of stroke in South Asia and neighboring countries seeking treatment from **MEDIKS International Hospital Islamabad PAKISTAN**

Lack of perceptiveness/unawareness on best possible control of preventable risk factors, secondary prophylaxis for patients with rheumatic heart disease, and admittance to knowledge and resources are noteworthy [148,149].

2.5 THE GLOBAL BURDEN OF CEREBROVASCULAR ACCIDENT

In general, the trends in stroke incidence and mortality rates have decreased in recent decades in developed countries (the United States, the United Kingdom, and Canada) [150,151]. This propensity may mirror both an improvement in risk factor control, as well as an improvement in life expectancy owing to reduced hypertension, hyperlipidemia, smoking reduction, and, in part, nutritional supplements. In addition, an improvement in acute stroke care may have led to an overall reduction in the percentage of stroke hospitalizations resulting in death in the United States [152,153]. While there have been reports of reduction in stroke

incidence and mortality in developed countries, the opposite has been observed in low to-middle income countries. However, the overall early stroke case fatality in low-to-middle income countries is found to be 25% higher than that seen in high-income countries in the past decade [154,155]. The cause for these differences are indistinct, however, in the low income case, patients are unlikely to have access to the same advancements in acute stroke care and secondary stroke prevention measures as seen in the high-income countries in the recent decades. Although advancement in stroke prevention and management has led to many successes in the fight against cerebrovascular disease for the past two decades, many challenges still linger to address, as clinicians and investigators try to uncover the underlying causes behind the many differences in stroke burden and outcome observed in epidemiologic studies to be able to design interventions to improve stroke mortality and disability for all [156,157].

3. MATERIALS AND METHODS

To find out the prevalence of risk factors in Pakistani stroke patients, we collected data from four hospitals concerned with treatment of patients with stroke (Combined Military hospital Nowshera, National Medical Center Nowshera KPK Pakistan, Yusra Teaching Hospital and Medipro Hospital Rawalpindi Pakistan) from August 01, 2016 till September 10, 2017. To ensure ethical soundness of the study, we received approval from the review boards at each

institution, and we did not collect identifying patient data.

Patients were asked to describe in detail where they got stroke and to speak a sentence of his native language, describe his /her name, visual acuity, ability to move his/her affected arm and leg as directed by the clinician. For patients who were incapable to speak, the account of their illness was given by the attendant(s). The data contained patient's clinical and biometric parameters (name, age, gender, living place, occupation), and presentation of risk factors for stroke such as, hypertension, diabetes mellitus, pregnancy, OCTP, obesity (overweight), smoking, heart diseases (ischemic heart diseases, rheumatic heart diseases, dysrhythmias).

We calculated descriptive statistics (totals and percentages) to estimate the percentages of the sample for the above mentioned risk factors.

To determine whether these incidences of risk factors differed between urban and rural populations in Pakistan, we calculated descriptive statistics (totals and percentages) for each of the relevant risk factors, stratified by urban/rural location.

Finally, to determine whether there is a difference between incidence of stroke in Pakistan and developed nations, we identified from literature review of stroke incidence figures for developed countries such as, France, Japan, the United Kingdom, the United States, Italy, and China. We calculated differences in the rate of stroke per 100,000 populations between each country and Pakistan [158,159]. Stroke incidence rates were sampled at various times depending on available literature, between 2006 and 2017.

4. RESULTS

Table 1 presents the demographic characteristics of the sample. The sample was predominantly female (64%), and the largest percentage of patients was between 55 and 65 years of age. Ever since Pakistan is not ethnically diverse, we present residence location and socioeconomic status to further characterize the sample. Participants were from all regions of Pakistan including those working /returning from abroad and their families, also some internationals (as shown in map), and were at or below middle class.

TABLE 1: SAMPLE DEMOGRAPHICS, N = 1,180

Variable	N	%
Female Age, n = 760		
14 - 22 years	76	10%
30 - 50 years	114	15%
55 - 65 years	152	20%
66 - 80 years	190	25%
81 - 100 years	228	30%
Male Age, n = 420		
14 - 22 years	21	5%
30 - 50 years	42	10%
55 - 65 years	105	25%
66 - 80 years	126	30%
81 - 100 years	126	30%
Residence Location, n = 1180		
Higher than sea level	283	24%
Plain area	897	76%
Socio-economic Status, n = 1180		
Below poverty to middle class	732	62%
Higher income	448	38%

4.1 INCIDENCE OF STROKE RISK FACTORS IN PAKISTANI STROKE PATIENTS

For the first research question, "What are the percentages of incidence of risk factors in Pakistani stroke patients?" we calculated descriptive statistics for our sample of 1,180 Pakistani stroke patients in Table 2. Results indicate that the most prevalent risk factor was Hypertension, which was found in 68.22% of our sample. This was the only risk factor present in over half of the sample. Risk factors appearing in between 1% and 3% of the sample included: Pregnancy/prolonged contraceptive use (2.97%), overweight associated with diabetes mellitus and hypertension (2.54%), smoking (2.71%), ischemic heart disease (2.03%), obesity/overweight (1.01%), Dysrhythmias (atrial flutter, atrial fibrillation) (1.01%) and valvular/Rheumatic heart disease (1.69%). Risk factors appearing in Diabetes mellitus is around 18%. Table 2 summarizes these results.

TABLE 2: PERCENT OF PREVENTABLE RISK FACTORS FOR STROKE PATIENTS, N = 1,180

Variable	n
Pregnancy/prolonged contraceptive use	35 (2.97%)
Overweight associated with diabetes mellitus and hypertension	30 (2.54%)
Smoking	32 (2.71%)
Ischemic heart disease	24 (2.03%)
Obesity/overweight	12 (1.01%)
Hypertension	805 (68.22%)
Dysrhythmias (atrial flutter, atrial fibrillation)	12 (1.01%)
Diabetes mellitus	210 (17.80%)
Valvular/Rheumatic Heart Disease	20 (1.69%)

4.2 DIFFERENCES IN STROKE RISK BETWEEN URBAN AND RURAL PAKISTANI POPULATIONS

The second research question asked, "Are there differences in the percentage patients with risk factors between urban and rural stroke patients?" To answer this research question, we calculated percentages for each risk factor, stratified by urban and rural location. Results indicated that the urban patients were more prone to all of the risk factors except valvular/rheumatic heart disease, where rural patients had a very slightly higher incidence. See Table 3 for a summary of results.

TABLE 3: STROKE PATIENTS (URBAN AND RURAL) WITH EACH PREVENTABLE RISK FACTOR

Preventable Risk Factors	Urban	Rural	Difference
Pregnancy/prolonged contraceptive use	20 (57.00%)	15 (42.86%)	14.28%
Overweight associated with diabetes mellitus and hypertension	19 (63.33%)	11 (36.67%)	22.66%
Tobacco use as smoking	19 (59.37%)	13 (40.62%)	18.75%
Ischemic heart diseases	16 (66.67%)	8 (33.33%)	33.34%
Obesity/overweight	8 (66.67%)	4 (33.33%)	33.34%
Hypertension	457 (56.77%)	348 (43.23%)	14.54%
Dysrhythmias (atrial flutter, atrial fibrillation)	7 (58.23%)	5 (41.67%)	16.66%
Diabetes mellitus	147 (70.00%)	63 (30.00%)	40.00%
Valvular/rheumatic heart disease	9 (45.00%)	11 (55.00%)	-0.10%

In Table 2, the most prevalent risk factor was Hypertension, which mirrors the same pattern in Table 3 where incidence was higher by 14.54% in the urban population compared with the rural population. The

prevalent risk factor for Diabetes mellitus patients was 40% higher in the urban population compared to the rural population. For other risk factors, the difference from 14% to 34% was more in the urban population compared to rural population.

4.3 COMPARING INCIDENCE OF STROKE BETWEEN PAKISTAN AND DEVELOPED COUNTRIES

To answer the third research question, “Is there a difference between Pakistani incidence of stroke and developed nations?” we compared rates per 100,000 population in Pakistan and seven countries. The stroke rate per 100,000 in Pakistan is 250[160,161]. The only country we examined with a higher rate of stroke was Germany, with an incidence of 350/100,000[162,163]. The remaining countries had lower stroke rates, with the exception of China, where the stroke rate was about the same as that in Pakistan (247/100,000 population)[164,165]. Table 4 summarizes these results.

Table 4: Comparison of Incidence of Stroke in Pakistan and Developed Countries (Rate/100,000)

Country/Region	Rate	Difference
Pakistan	250	
Germany	350	-100
Italy	223	27
UK	161	89
France	114	136
US	200	50
Japan	130	120
China	247	3

5. DISCUSSION AND CONCLUSIONS

Our results yield some novel information about stroke risk factors in Pakistan. Most interestingly, besides hypertension pregnancy and (OCTP) use was also a notable risk factor, in our sample. [166,167,168].

This urges to design added best practices and interventional strategies for stroke management in Pakistan. This in particular, heart health and stroke prevention among pregnant and sexually active women using OCTP deserves an increased focus. Owing to the scarcity of data on stroke risk factors and epidemiology in Pakistan, further research is warranted to confirm our findings and understand more about the reasons for the high incidence of pregnancy OCTP use as a risk factor for stroke [169,170,171].

Second, our study indicated that, in most cases, risk factors have some degree of dissimilar prevalence rates among urban and rural populations. It is notable to say that pregnancy and OCTP have an impact factor relatively more in urban than rural populations [172,173,174].

There could be several explanations for this finding.

First, it could reflect lower rates of OCTP among rural Pakistani population, either because of less availability, or moral issues. With use, it could reflect conflicting lifestyles among pregnant and sexually active women using OCTP between urban and rural Pakistani populations. Further research will be required to clarify this finding and control for confounding variables[175,176,177]. It is important to ensure that OCTP by Pakistani women of child bearing age are safe for prolonged use. At the same time, poor updated knowledge of local physicians not associated with tertiary care setups contributes towards the use of obsolete and relatively less effective medical healthcare delivery [178,179,180]. Ignoring the burden of stroke may have health and economic consequences.

In conclusion, our international comparative data are interesting in that they reveal a high incidence of stroke among Pakistani patients compared with most developed countries. This suggests an increased need to emphasize research and intervention for stroke, in order to reduce the disease burden in Pakistan. This study is subject to certain limitations, which readers should take into consideration when interpreting our results. First, our data lack specificity regarding demographic data, lifestyle factors, and other information that could shed light on the incidence of risk factors, particularly among women. Second, we present only descriptive data, so we do not make claims regarding the statistical significance of our findings. Finally, our international comparison data are drawn from a small sample of studies across over a decade of time. More recent, robust, and directly comparable data will be needed to confirm and strengthen any conclusions made on the basis of these international differences [181,182,183]

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