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The Sub-Standardized Approach to Stroke Management in Low and Middle-Income Countries Including Pakistan: Limitations and Suggested Options to Overcome Some of the Shortcomings Via Teleneurology/Telestroke Application

Rizwana Shahid
Imam AbdulRahman bin Faisal University, Dammam, Saudi Arabia

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THE SUB-STANDARDIZED APPROACH TO STROKE MANAGEMENT IN LOW AND MIDDLE-INCOME COUNTRIES INCLUDING PAKISTAN: LIMITATIONS AND SUGGESTED OPTIONS TO OVERCOME SOME OF THE SHORTCOMINGS VIA TELENEUROLOGY/TELESTROKE APPLICATION

Rizwana Shahid[1]
[1]*Imam AbdulRahman bin Faisal University, Dammam, Saudi Arabia*

Corresponding author: ***Rizwana Shahid*** *Departement of Neurology, College of Medicine, Imam Abdulrahman Bin Faisal University, Dammam, Saudi Arabia* ***Email:*** *rshahid@iau.edu.sa*

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ABSTRACT

Background and objective:

Ischemic stroke still poses a significant health concern throughout the world. However, low and middle-income countries (LMIC) in Asia have more devastating outcome. The vascular risk factors are prevalent in most parts of Asia, contributing to increasing incidence. The recommended approved treatment for acute stroke is limited to a few areas in these countries. We aimed to identify stroke risk factors, its incidence and prevalence; treatment opportunities offered in various parts of the region and utilizing the alternate pathways to improve the disease recognition and management outcome.

Method:

A comprehensive search using PubMed, MEDLINE, Medline Plus, PubMed Central and Pak Medinet, including the various key words was performed,

Results:

Two-hundred-fifty-five articles of potential interest were found through the initial search. The studies were analyzed in detail in order to obtain relevant information according to the objectives of the review. Most of the literature was regarding the stroke risk factors. Only few articles regarding the current status of stroke services and management options in LMIC were available.

Conclusion:

Some of the factors identified in previous studies preventing the utilization of recent advancement in the diagnosis and management of stroke in LMIC, including Pakistan, were lack of awareness of stroke symptoms among general population and physicians, poor knowledge of management options, unavailability of trained stroke neurologists, poor infrastructure, cost effectiveness and patients' trust more on homeopathic physicians, quacks and spiritual healers instead of medical doctors. Stroke is still managed conservatively in most part of these countries. There is strong need of alternate means to overcome these shortcomings in managing this highly morbid condition. As only few studies specifying the prevalence and management outcome in LMIC including Pakistan are available, a strong database is needed to quantify the real burden.

Key words: Stroke, Low and middle-income countries, Pakistan, Management, Telestroke.

INTRODUCTION

The incidence of non-communicable diseases has increased drastically and stroke is emerging as a primary cause of disability and vascular death worldwide, including Asia.[1] The incidence of vascular diseases is higher in low and middle-income countries (LMIC). The World Bank assigns the world's economies to four income groups, low, lower middle, upper-middle, and high income. The classifications are updated each year on July 1 and are based on the gross net income (GNI) per capita of the previous year (2022).[2] As of 1 July 2022, low-income economies are defined as those with a GNI per capita, calculated using the World Bank Atlas method, of $1,085 or less in 2022; lower middle-income economies are those with a GNI per capita between $1,086 and $4255; upper middle-income economies are those between $4256 and $13205; high-income economies are those with a GNI per capita of >$12,376.As per this classification, Pakistan is classified in lower middle-income income country.[2]

Stroke also affects the quality of life and average mortality rate is higher in Asia as compare to America, Europe, Australia and other western countries, making it a serious problem.[3,4] This becomes especially important when under development meets major bulk of the world population. Incidence of stroke is estimated to be around 70%, stroke related deaths 87% in low, and middle-income countries.[3,4] The prevalence of vascular risk factors is considerably high in LMIC in Asia, directly affecting the incidence and prevalence of stroke. The treatment options are limited, which could be the result of unaffordability due to low socioeconomic status or lack of proper infrastructure to facilitate time dependent management of acute stroke. Another contributing factor hindering the acute stroke management in LMIC is lack of awareness regarding the stroke symptoms among the general population and even many physicians. Shortage of neurologists and specialized stroke physicians is another major reason in the management of goal directed specialized stroke treatment. As it is very difficult to get the information individually from each country, we tried to get general information from LMIC in Asia with particular emphasis on Pakistan. We were unable to find the large-scale epidemiological studies. In fact, only few articles discussed the status of available treatment options in Pakistan. We propose that the utilization of telemedicine service may benefit acute stroke patients tremendously who would otherwise be unable to receive acute stroke care because of unavailability of stroke physician or related infrastructure.

METHODS

Data Sources: A comprehensive search of the published literature was conducted using PubMed, MEDLINE, Medline Plus, PubMed Central and Pak Medinet.

Various search terms including the 'cerebrovascular accident, acute ischemic stroke, recombinant tissue Plasminogen Activator, window period, feasibility, stroke in developing countries, Pakistan, stroke management, stroke rehabilitation, telestroke, telemedicine' were used.

Article screening:

Author first categorized articles as relevant or irrelevant by screening the abstract. Articles were included focused on stroke risk factors, prevalence and management options in these LMIC with special consideration to Pakistan.

Study Selection: The initial search revealed 255 articles of potential relevance.

Data Extraction: Author in detail analyzed the studies, in order to obtain the clinical information relevant to meeting the objectives of the review.

Data Synthesis: Author grouped articles according to topic and types of studies within each group. Abstracts were reviewed initially in order to match the relevance and then full text articles matching our selection criteria were extracted and reviewed.

Inclusion criteria: Articles relevant to our study objectives from the LMIC of Asia , as described previously, were included.

Exclusion criteria: We excluded the articles from Middle Eastern countries as they differ from LMIC of Asia in different aspects such as ethnicity, health care infrastructure, natural resources to name a few. Therefore, their infrastructure and health care does not represent our targeted population.

Results: Initially, 255 articles were identified through various search engines as described. For greater specificity only those articles referencing vascular risk factors, disease burden and management options and utilization of telehealth services were selected. Duplicates were excluded. Articles not addressing question were excluded, This yielded 200 articles. A total of 55 articles specific to the set objectives were selected and analyzed for review writing.

A single author (RS) conducted the entire data search.

The data were then organized according to our relevant topic.

EPIDEMIOLOGY OF STROKE IN ASIA

Despite a gradual decline of the stroke incidence in western countries, the Asian countries have seen a gradual increase in the incidence and prevalence of stroke.[3,5] Cerebrovascular diseases are a cause of major concern especially in Asia, as it has more than 60% of the world's population. Some researchers have reported the stroke rates to be five to ten times higher in India, Pakistan, Russia, China, and Brazil in comparison to United Kingdom or the United States.[6,7] This high prevalence of stroke, which is considered highly morbid and causing long-term disabilities in most of the survivors, causes the expenditure of resources due to finances, loss of work force and health services compromise. The stroke related deaths in these countries were around 75.2% of all stroke related deaths and 81% of associated Disability-adjusted life years (DALYs) lost.[8]

Asia is facing special problems regarding stroke management and rehabilitation. Due to lack of resources, stroke mortality is higher in Asia as compared to Americas, Western Europe and Australasia, with the exception of few countries like Japan. Asia has higher but variable stroke burden, in comparison to western countries.[9] As per 2010 statistics, the high-risk stroke cost per capita for patients reached up to $517.8 per year in China, while a review conducted in 2019 compared the stroke cost in Indonesia, Malaysia and Singapore and they found the cost among these 3 countries to be high variable as $ 135.55 per day care (3.88% of GDP per capita in Indonesia, $277.53 per day (2.11% of GDP per capita) in Malaysia while Singapore had per day care cost of $ 366.67 (0.65% of GDP per capita).[10,11] As stroke care cost is very high, it creates a huge economic burden on already compromised economies of LMIC, it is crucial to give more attention and have more effective health care planning, especially in the primary and secondary stroke prevention as well as the early detection of disease is warranted.

STROKE RISK FACTOR IN ASIA

As we have observed previously, stroke has very significant impact on economy as well as the quality of life for patient itself and for the whole family, it is very important to identify the risk factors as 74.2% of the risk is attributed to modifiable risk factors that can be altered with the life style modifications.[12-14] Eastwood SV et al have reported that south Asians had a high prevalence of dyslipidemia, central obesity and diabetes mellitus and had a twofold higher risk of suffering from stroke in comparison to Europeans.[13] This risk secondary to ethnicity was also observed in another study conducted by Wen Lin Teh and his team, where Malay people were at lower risk of stroke (OR=0.4) than the Chinese people.[15]

SPECIFIC CONCERNS RELATED TO STROKE AND NCD IN PAKISTAN

Pakistan is a developing country in South Asia, being the world's fifth populous country, with a population of around 227 million.[16,17] According to current population statistics, it is estimated that Pakistan will reach its peak population in 2092 of 404.68 million and its population is expected to surpass Indonesian population by the year 2048, with the estimates of around 331.29 million.[18.19] The global burden of the disease 2010 statistics has reported that non-communicable diseases (NCDs) accounted for 77% of the age-standardized deaths.[20] In a study conducted by Jaffer T in 2006, the prevalence rate of stroke was around 4.8% translating into 4 million people.[21] While the lifetime prevalence of stroke symptoms in Pakistan has been reported to be about 19%, with an estimated seven million persons being affected. Large-scale epidemiological studies regarding the stroke incidence are lacking in Pakistan. According to the study conducted by Ali Zohair Nomani, the estimated annual incidence of stroke in Pakistan is 250/100000.[22] The prevalence of chronic medical conditions like diabetes and hypertension is very high in Pakistan and majority of patients are unaware, mainly due to lack of routine medical checkup, unavailability of screening services at the local clinics and overall ignorant behavior of the community towards their personal health.[23] Even the patients with known vascular comorbidities, the regular follow up or the compliance to the regular checkup is very poor, further complicating the situation. The decline in the incidence of stroke in developed countries is in part a reflection of risk factor control as well as in improvement in life expectancy secondary to reduced incidence of hypertension, dyslipidemia, smoking reduction and in part due to nutritional supplementation.[24] The burden of risk factors for stroke is also rising in Pakistan, it was estimated that by 2020, Pakistan would be the 4th most populous country having diabetes; annual incidence for diabetes was estimated to be 250/100000, which is approximately 350000 new cases each year.[25] The ideal stroke care is defined in figure 1.

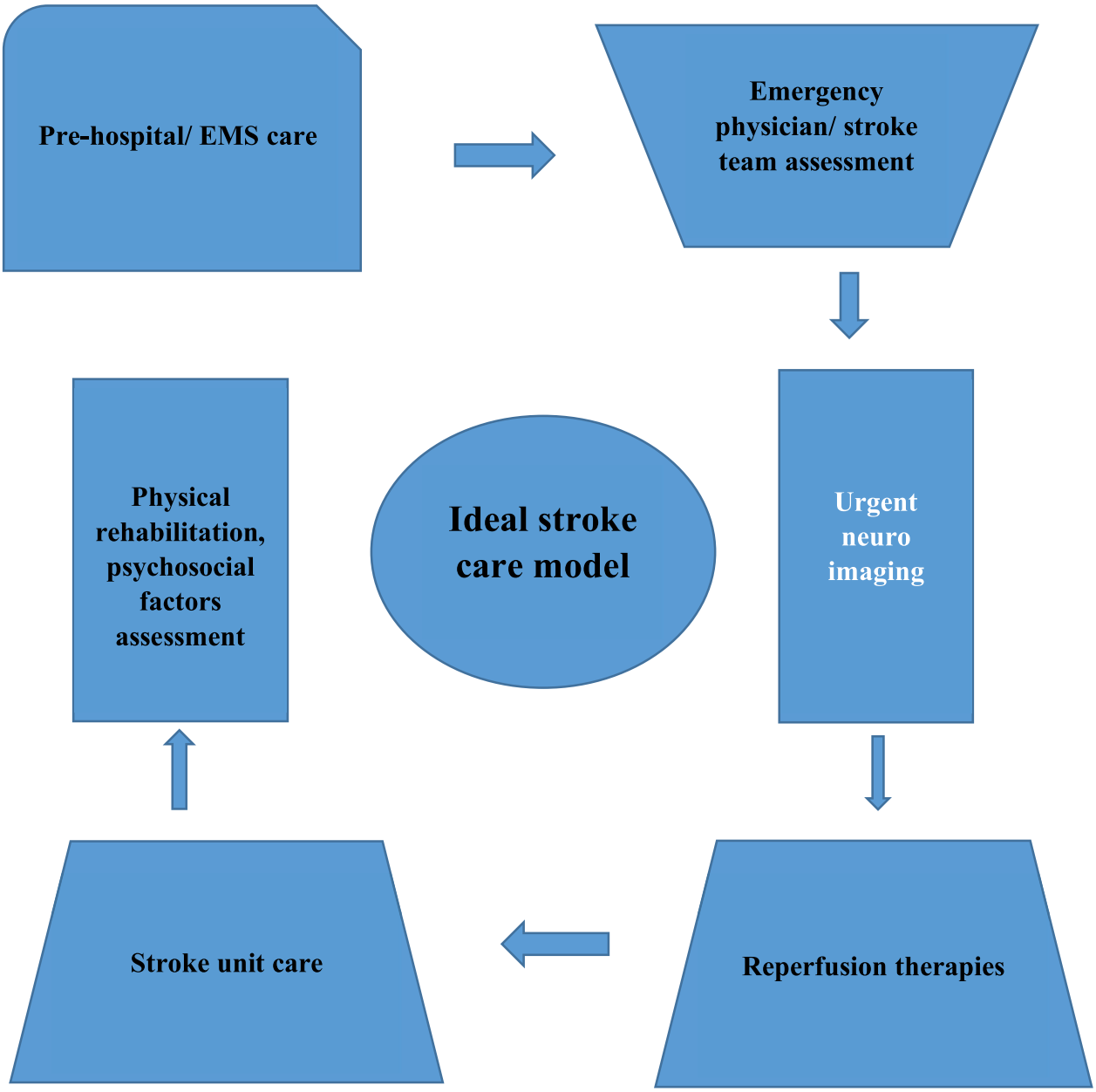

Figure 1: ideal stroke care model

NEUROLOGY/ STROKE SERVICES IN PAKISTAN

In many underdeveloped countries, neurology is still not recognized as a separate entity, rather considered as a part of internal medicine training.[26] This is the case in parts of Pakistan as well, where the patients with neurological diseases are admitted under internal medicine services and neurology, per se, is still underappreciated and under recognized as a separate subspecialty.[27,28] The first structured clinical and academic neurological training program in Pakistan was introduced in 1960 in two major cities of Pakistan. Two training centers were established; one in Karachi with a combined neurology and psychiatry department program and another one in Lahore. Separate neurology department still do not exist in many of the Pakistan's premier medical colleges.[26-28] A report published in Pakistan journal of Neurological Sciences in 2011 identified only 15 out of 72 medical colleges having a neurology department or neurology faculty. Most of graduating medical students from these colleges do not get a structured neurology teaching. [29]

ACUTE STROKE MANAGEMENT IN LMIC

As acute stroke thrombolysis with IV tPA (tissue plasminogen activator) is the cornerstone for treatment after the National Institute of Neurological Disorders and Stroke (NINDS) trial, which has significant impact on reducing the mortality and morbidity, but the number of stroke patients receiving recombinant tissue plasminogen activator (r-tPA) in the developing world is extremely low.[30] The reasons for non-treatment are manifold, including the pre-hospital delay due to lack of awareness of stroke symptoms, financial constraints and lack of infrastructure. This prevents access to the health care facility in timely manner. According to one analysis regarding thrombolysis in developing countries, the percentage of stroke patients' arrival to ER (emergency room) within three hours of symptom onset was 8% in Iran and 14.7% in India.[31, 32]

Transient ischemic attacks (TIAs) pose a significant immediate risk of stroke (around 10%) in first 90 days, the initial 48 hours being the most critical, so the early recognition and intervention after TIA has 80% relative risk reduction in the emergence of stroke in western cohorts. Research from Pakistan have reported almost similar statistical results regarding risk of stroke after TIA, but the revolutionary treatment adopted in western countries post TIA is still very premature in Pakistan, further contributing to the stroke risks. Low to middle-income countries observe around 25% higher stroke case fatality in comparison to high-income countries.[22]

ACUTE STROKE MANAGEMENT IN PAKISTAN

The current stroke management protocol approved by American heart association (AHA) involves intravenous thrombolysis up to 4.5 hours window and endovascular treatment in strokes secondary to large vessel occlusion.[33] As per the review article published in 2017, only two centers were equipped with the facility for emergency room triage of thrombolysis in acute stroke and TIAs, and these centers also have very limited number of cases so far.[22] Another factor contributing to poor stroke treatment response in Pakistan is patients' inclination towards using the homeopathic medications, herbal remedies, visiting quacks and a strong belief on spiritual healing, besides seeking treatment from a medical doctor.[34] Emergency medical services (EMS) are not trained to recognize acute stroke and therefore unable to triage and pre-alert hospital systems. This is especially true in rural areas.[34] As per Hashmi et al in 2013, there were only 60-trained neurologists in Pakistan for 160 million population and most of them were concentrated in 15 hospitals in seven major cities. Only five hospitals have stroke units, only one interventional radiology program and no rehabilitation center for post stroke rehabilitation.[35] A major contributing factor, which may have led to reduction in stroke, related hospitalization and death in developed countries, is their improvement in acute stroke care. [36]

CURRENT ADVANCEMENT IN ACUTE STROKE MANAGEMENT IN PAKISTAN

In a recent report, the chairperson of Pakistan Stroke Society mentioned about the recent advancement adopted for acute stroke care in Pakistan. Some of the methods adopted to facilitate the management of acute stroke patients include a rescue transport facility, named 1122, with well-equipped and trained staff for managing the acute cardiovascular events in major cities of Pakistan. However, as the knowledge regarding the stroke symptoms and management is limited among the public and paramedics, its implication is still limited. As per the current report published in 2021 by the president of Pakistan Stroke Society, approximately 10 stroke units in different cities of Pakistan were established, out of these, only six centers are offering intravenous thrombolysis (recombinant tissue plasminogen activator, r- tPA).37 The major hindrance for patients' ability to access acute stroke care at a private, tertiary care center is the cost of care in the stroke unit in Pakistan, as public health facilities are not capable of providing acute stroke management due to severe shortage of health budget. Lack of proper infrastructure is another hindrance in referral to the properly equipped stroke centers.[37, 38]

ROLE OF TELEMEDICINE IN ACUTE STROKE MANAGEMENT

As acute stroke treatment options are highly time dependent, the problem further supplemented by a growing shortage of specialized clinicians. Stroke management needs innovative ideas for improving the patient outcome due to this debilitating disease. Teleneurology is one of these modern innovations that have been proven to improve the outcome of stroke.[39] Based on American Heart Association guidelines, telestroke has been proven as a valid tool for acute stroke assessment and it is being successfully utilized in stroke clinic and emergency room settings for many years in the developed countries.[40,41] By the virtue of teleneurology/telestroke services, there is a better chance of patients living in the medically underserved areas to receive the timely and consistent care as it provides the ease of access to neurological care, which in turn is helpful to overcome the physician shortage and improve the continuity of care by reducing unnecessary transfers and testing by non-trained neurologist/ vascular neurologist.[42] Covid-19 crisis has

significantly highlighted the importance of telemedicine and there is significant advancement in the usage of telemedicine services during the past two-years.[43] By using telemedicine services, patients in the remote or under privileged areas have access to both primary and specialized care and at the same time, it minimizes the travel and reduces physician contact. Thereby, electronic consultation is extremely helpful in delivery of outpatient healthcare without compromising the specialty expertise in remote areas.[42] The concept of telemedicine involves either indirect contact of a physician in peripheral hospital with another subspecialty consultant for their expert opinion or direct contact of physician with the patient in the remote area through video conference.[43-45]. Stroke medicine is considered a highly specialized field, which requires immediate steps for appropriate management. Usually a teleconsultation is between a physician working in remote area or primary health care setting, with a stroke physician working in a tertiary care center.[43,44] The revolutionized management of acute stroke in developed countries, with the availability of IV thrombolysis for hyper-acute stroke and extended window period for mechanical thrombectomy in eligible patients up to 24 hours has significant impact on the outcome of the patients. However, as these treatments are highly time dependent and specialized trained staff is needed for the implementation; situation is still not so promising in under developed countries. Only few hospitals offer the IV tPA for acute ischemic stroke patients. Most of the stroke patients are managed by internal medicine physicians without the consultation by a neurologist. Furthermore, endovascular thrombectomy (EVT) is almost nonexistent because of the unavailability of the trained EV surgeons the limited availability of radiological facility like CT, MRI further compromises the acute stroke management. The proposed comprehensive tele stroke model is described in Figure 2.

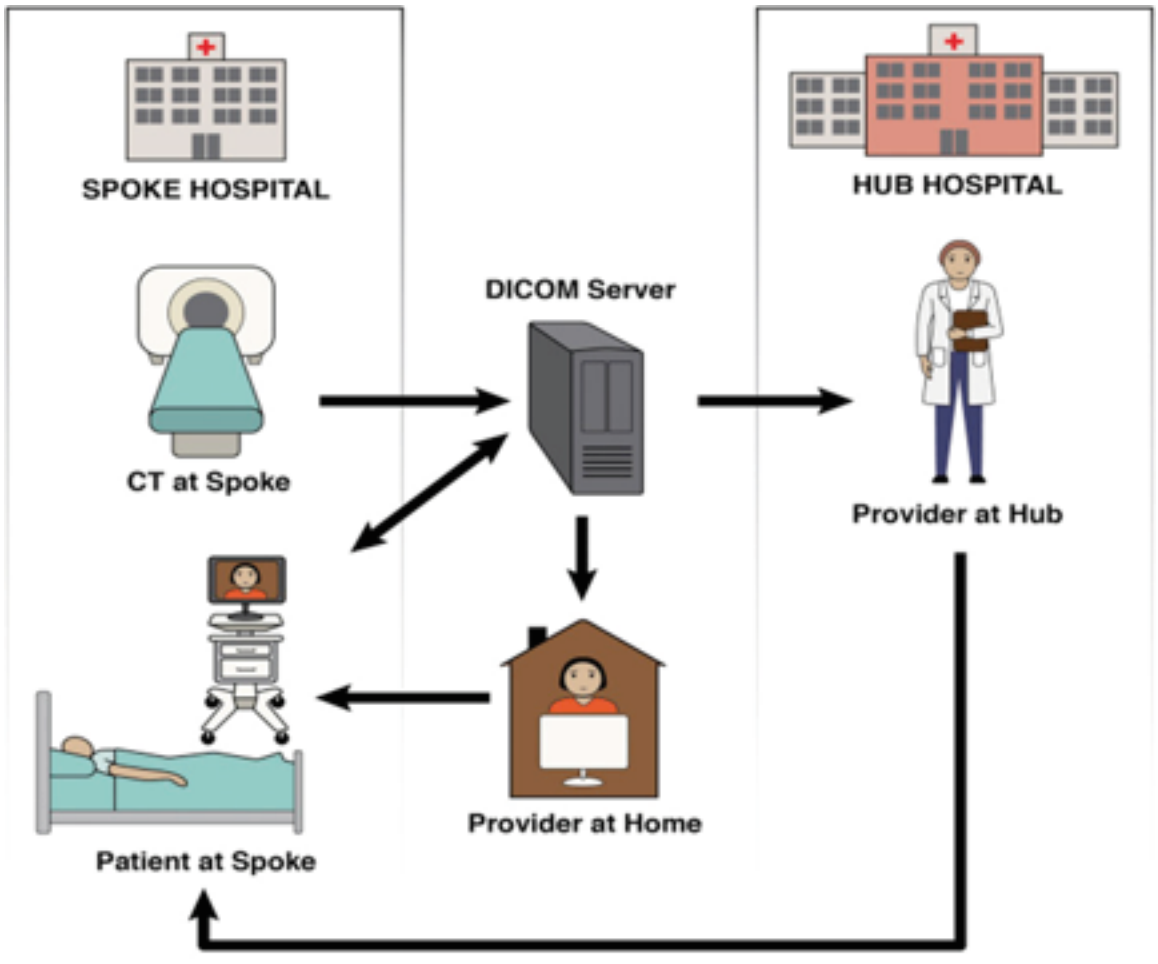

Figure 2: Comprehensive telestroke model

QUALITY OF LIFE AFTER STROKE IN UNDERDEVELOPED COUNTRIES

Stroke survivors were interviewed in a study by occupational department, Edmonton, Canada. The results of the study revealed most of them were young but depressed and suffering from the increased functional dependence and with neuropathic pain.[46] According to few qualitative studies performed in Pakistan, the caregivers of stroke survivors were found to be isolated and frustrated as well as the element of financial crisis and physical burden was very prominent factor. The caregivers demanded to have a responsive health care system to ease their burden.[46, 49]

Stroke has devastating consequences on the quality of life as it impairs the social, physical and psychological aspects of the patients.[50-53] Quality of life is the patient's image about himself or herself in relation to their culture and value system and in the context to fulfill their goals, expectations and concern. However, the data is very sparse about Quality of life (QOL) from low and middle-income countries.[53] Recent researchers have found that the traditional stroke risk factors like hypertension and diabetes are increasing in Asian countries and the stroke burden is following a similar trend. According to study published by Valery L Feign in 2013, Pakistan had an alarming percent of population suffering either from DM, HTN or both.8 Qureshi et al have reported the current prevalence of diabetes in Pakistan to be around 9-10%. Even the prevalence of pre-diabetes is much higher in Pakistan in comparison to the western countries. An overall prevalence of hypertension was estimated to be 19% in people aged 15 years or higher. Obesity prevalence rate in south Asia is ranging between 20-30% and their body mass index has lower cut off value for quantification of disease like diabetes and cardiovascular diseases, adding further to the vascular risk factors.[54, 55]

SUGGESTED OPTIONS TO IMPROVE THE STROKE MANAGEMENT AND QUALITY OF LIFE IN STROKE SURVIVORS

- As vascular risk factors are prevalent and most of the population is unaware about their comorbid, pre-screening and awareness campaigns should be encouraged to minimize the incidence of stroke.
- Awareness regarding the stroke symptoms and treatment options should be stressed through mass campaigns; programs can be organized at hospitals and public places of common interest like shopping malls, mosques, parks etc.
- Paramedical staff must be trained regarding the stroke symptoms and available therapies, as they are usually the first encounter with the patients.
- More training centers for neurology and stroke are needed to meet the demands of growing population.
- Trained neurologists and stroke neurologists need to be on board to implement the acute stroke care pathway.
- Organized stroke centers capable of implementing acute stroke care must be established at accessible locations in major cities.
- Tele stroke consultation may be adopted to overcomethe gap in peripheral or inaccessible locations.
- Rehabilitation and psychological support must be available to stroke survivors to improve the QOL

STRENGTH AND LIMITATIONS

We tried to address the obstacles and hindrances in the management of acute stroke care in LMIC. We found many articles regarding the stroke risk factors and symptoms but data is lacking regarding the utilization of newer treatment options adopted in western countries for hyper-acute stroke management. Very few articles discussed the stroke services and thrombolysis and mechanical thrombectomy status in this region. We tried to give new insights to the clinician about utilization of tele stroke model to overcome the shortage of trained physicians. Through this model, the stroke services can be extended to many remote areas, from where patients cannot reach the highly specialized centers due to time constraint and poor infrastructure.

CONCLUSION AND RECOMMENDATION

Stroke is a serious non-communicable disorder affecting significant number of the population around the globe. As there are only few studies specifying the prevalence and management outcome in LMIC including Pakistan, a strong database is needed to quantify the real burden.

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