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RISK FACTORS OF HUMAN RABIES IN SOUTH ASIA: A SYSTEMATIC REVIEW

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ABSTRACT

Background

Rabies as a zoonotic viral disease is one of the neglected tropical diseases with high incidence among the poorest communities of least developed and developing countries of Africa and Asia.

Aim

This study aims to investigate the risk factors of human rabies in south Asia, with focus on Bangladesh, India and Pakistan.

Method

A systematic review approach was adopted, which included studies that identified the risk factors of human rabies in the three south Asian countries from 2007 to 2016. Electronic databases searched include PsycINFO, PubMed Central [PMC] and Cumulative Index of Nursing and Allied Health Literature [CINAHL]. Appropriate data screening was carried out to extract relevant articles. Finally, the articles were quality appraised and synthesized with a narrative synthesis approach.

Result

Eight relevant studies were finally identified, with either moderate or high quality. The studies identified one or more risk factors of human rabies. The findings include; animal bite mostly from certain stray animals (dog, cat, monkey and rat). Secondly, poor knowledge/awareness of the people about human rabies, thus people were ignorant of the need to seek for immediate treatment following animal bites. Thirdly, poor traditional/cultural practices following bites from infected animals. Fourthly, socioeconomic factors and finally, poor use of preventive measures against rabies.

Conclusion

Based on the findings, it is concluded that most of the factors predisposing to rabies infection in south Asia are preventable, hence; Government authorities, non-governmental organizations and philanthropists should be more committed toward increasing awareness about the consequences of the infection as well as providing free and accessible treatments across each country.

Keywords: risk, factors, rabies, Bangladesh, India, Pakistan

1.0 INTRODUCTION

Rabies is a worldwide veterinary and public health problem most especially in the least developed and developing countries of Africa and Asia (Yin et al., 2013). About 3.9 billion people are at risk of rabies infection worldwide, with more than 7 million people treated for rabies and 50 - 55 thousand people die due to rabies infection each year in more than 150 countries of the world (Hampson et al., 2007; Hampson et al., 2009; Piyaphanee et al., 2012; Yin et al., 2013; WHO, 2017). It is a zoonotic viral disease caused by an RNA Virus family (Rhabdoviridae) that has dog as one of its major host, alongside jackals, foxes and wolves (Chowdhury et al., 2015; Hampson et al., 2015; Devleesschauwer et al., 2016). Although rabies has a high worldwide fatality rate, but it can be 100% preventable and is termed as one of the neglected tropical disease with high incidence among the poorest communities in the least developed and developing countries of Africa and Asia (Gongal and Wright, 2011; Madhusudana et al., 2011; Nel, 2013). Dog bites are the major cause of human rabies in all the rabies endemic countries and results in 96% of rabies cases in Southeast Asia (Gongal and Wright, 2011). Therefore, prevention and control of rabies depends on eradication of dog rabies. Similarly, more than 1.4 billion people are at risk of rabies in southeast Asia and between 23 to 25 thousand people die due to rabies infection, accounting to about 45% of world fatality rates due to rabies (Dodet et al., 2008; WHO, 2017).

The South Asia rabies endemic countries are categorized into 3 groups based on the burden of the disease as either high (India, Pakistan and Bangledesh), medium (Bhutan, Nepal and Sri Lanka) and low (Afghanistan) (Chowdhury et al., 2015; Gongal and Wright, 2011). Bangladesh death rate for human rabies, is estimated at about 2,000-2,500 deaths per year (Hossain et al., 2011), Between 1990 to 2002, human rabies deaths in India is estimated at about 30 000, accounting for nearly 60% of global mortality (WHO, 2002) but recently, human rabies death rate is estimated at about 19,000 annually in India (Marathe and Kumar, 2016), while the mortality rate from rabies infection in Pakistan is estimated to be between 2000 to 5000 deaths annually (Knobel et al., 2013).

The current statistics on Rabies infection in the three high burden countries (Bangladesh, India and Pakistan) suggest that there is an existing gap in curbing the disease. A systematic review of the risk factors associated with rabies infection in these regions is of utmost importance as it will point out the factors that promote the disease, thereby strategizing ways of controlling and preventing the future occurrence of the disease by creating awareness on the risk factors of the disease and the preventive measures. Any knowledge added to what is currently available will be relevant because such knowledge can inform policy directed toward eradicating the disease. Therefore, the aim of this study is to investigate the risk factors associated with human rabies infection in three selected South Asian countries i.e. Bangladesh, India and Pakistan.

2.0 METHODS

2.1 Study Design - Systematic review approach was adopted in conducting this study due to availability of some primary studies in this field. It was conducted based on established inclusion and exclusion criteria (Table 1).

Table 1: **Inclusion and Exclusion Criteria**

Inclusion criteria	Exclusion criteria
Primary research studies	Secondary research studies/review studies
Studies conducted in Bangladesh, India or Pakistan or south Asia as a whole	Studies conducted outside South Asia
Studies that identified risk factors of human rabies	Studies that do not identify risk of rabies infection
Studies published in English language	Studies published in other languages than English
Studies of moderate to high methodological quality	Studies of low methodological quality
Studies published from 2007 to 2016	Studies published before 2007

Studies within the past 10 years (2007 to 2016) were considered to ensure that only recent studies provide evidence for this review.

2.2 Search and Screening Strategies – Duplicate searching and screening were done by the first and second authors. Three databases were searched, which include; PsycINFO, PubMed Central [PMC] and Cumulative Index of Nursing and Allied Health Literature [CINAHL]. Search terms for the study were identified by running the research topic the MeSH term website, which gave the alternative search terms available for the subject matter. Hence, the following search terms were used to search relevant articles for this study, which were combined with Boolean operators ‘OR’ ‘AND’. The first category of the search term used relates to the predisposing factors, and they are: ‘Risk factor’ ‘causes’ ‘predisposing factor’. The second category which relates to the condition under investigation are: ‘Rabies’ ‘Infection’ ‘dog bite’ ‘animal bite’. The third category which relates to the location is: ‘Asia’ ‘South Asia’ ‘South east Asia’ ‘Pakistan’ ‘Bangladesh’ ‘India’. After the application of the search terms into the various databases and the search result obtained, a two stage screening were adopted. Firstly, the articles were screened based on the tittle and abstract in accordance with the eligibility criteria. Secondly, the articles that scaled through the first step undergo a full text screening against the inclusion

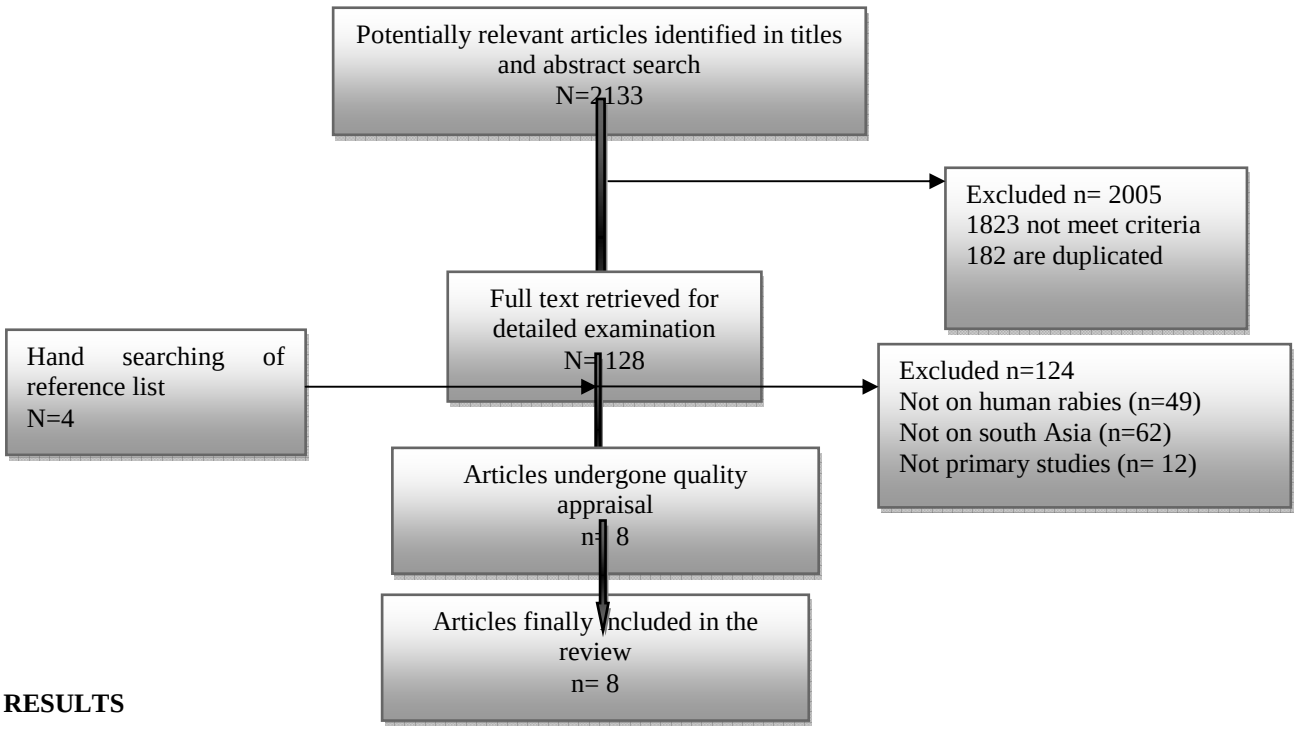
and exclusion criteria.

2.3 Data Extraction - The data extraction is done by the second author and cross checked by the first author for accurateness. For this purpose, a template is designed in line with PRISMA checklist using a spread sheet package. The information extracted are those that relates to the authors details, publication dates, tittle and aim of the study, the study design used as well as outcome measures of the included studies. Other information includes; quality assessment score for the studies, methods of analysing data, main result/findings as well as the authors' conclusion.

2.4 **Quality Appraisal -** For this study, an appraisal tool formulated by Downs and Black (1998), modified by Kennelly (2011) was used for this purpose. The appraisal instrument is made up of three sections; they are: quality of the reporting, validity of the methods used and lastly the accuracy of reporting the research study findings. A total obtainable mark of the entire question is 34. Based on the total points accrued, the quality of the research article is graded as strong evidence (≥ 20 points), moderate (15-19 point) and weak when it is less than 14 points.

2.5 Data analysis - Based on the heterogeneous nature of the studies that met the inclusion criteria of the study, a thematic analysis approach was adopted rather than met-analysis. The results of the studies were therefore grouped in to themes and for more clarity into sub themes in some cases to make discussion easier. Accordingly, eight studies (Figure 1) completely met the selection criteria and were used in analysis.

Figure 1: Search Results using Modified PRISMA Flow Chart



3.0 RESULTS

3.1 Summary of the selected studies

The 8 studies that met the inclusion criteria are Hundai et al., 2016, Zaidi et al., 2013, Dey et al., 2011, Joseph et al., 2014, Sharma et al., 2016, Ghosh et al., 2016, Wasay et al., 2012 and Dodet, et al., 2008. All the studies were conducted in one of the south Asian countries of Pakistan, Bangladesh or Indian, except one (Dodet, et al., 2008)

which was conducted on 8 Asian countries including the three countries of interest (Pakistan, Bangladesh or Indian). Three of the studies (Hundai et al., 2016, Zaidi et al., 2013 and Wasay et al., 2012) were specifically conducted in Pakistan, two studies (Dey et al., 2011 and Ghosh et al., 2016) in Bangladesh, and the other two (Joseph et al., 2014; Sharma et al., 2016;) in India. All the studies used cross-sectional surveys using interviews and/or questionnaires and the risk of contracting human rabies infection is well established. Of the 7 studies that are country specific, only one (Zaidi et al., 2013) look at Geographical differences within the country of Pakistan. Dodet et al., (2008) study on the other hand looked at wider geographical differences between 8 countries of Asia, which include Bangladesh, China, India, Indonesia, Pakistan, the Philippines, Sri Lanka, and Thailand. Specific detail of each study is summarized in table 2.

3.2 Population of the study

Both male and female participants from all age groups were included in all the studies except Dey et al., (2011), who specifically focused on pediatric population. Participants from two studies (Hundai et al., 2016 and Zaidi et al., 2013) were respectively from Punjab and Karachi areas of Pakistan. Participants in Dey et al., (2011) study were patients diagnosed with rabies infection, most of which are between the ages of 5 to 10 (44%), while 33% were less than 5 years of age and 23% above 10 years of age. Study of Joseph et al., (2014) investigated 200 participants, most of which are males (67%) as against females. Children less than 18 years accounted for about half of the participants (51%) and the average age of all participants was 18years. Sharma et al., (2016) studied 2887 participants sampled from 500 households, most of which have attended school and are from nuclear family. The mean age of the respondents who had dog bites was 21.5 years. In the study of Gosh et al., (2016), 3200 participants were selected, each from a household, out of which males accounted for 90% of the population. The participants had an average age of 35years and 9% of them own at least 1 dog, of which 5% were sterilised. Wasay et al., (2012) study investigated 1201 participants, of which males were 65% against females. The age of the respondents range from 18 to 86, with an average of 31±13 years, and most of them were educated to secondary level or more. Dodet et al., (2008) study included a total of 4377 participants from the 8 eighth Asian countries, out of which Bangladesh (750), India (569) and Pakistan (519) constitute 42%. The ratio of males to females is 1.6 to 1, with a mean age of 27 years.

Table 2: Summary of Included Studies

S/N	Authors and year	Title of the study	Aims/objectives	Designs	No. of part	Data analysis	Key findings	Conclusion	Qual. ranking
1	Hundai et al., 2016	Awareness, knowledge, and risks of zoonotic diseases among livestock farmers in Punjab	The present study was conducted to assess the awareness, knowledge, and risks of zoonotic diseases among livestock farmers in Punjab	Crossectional Survey	250	ANOVA using SPSS version 16	The findings indicated about 84.8%, 46.0%, 32.8%, 4.61%, and 92.4% of livestock farmers were aware of zoonotic nature of rabies, brucellosis, tuberculosis, anthrax, and bird flu, respectively. The 55.6%, 67.2%, 52.0%, 64.0%, and 51.2% respondents were aware of the transmission of zoonotic diseases to human being through contaminated milk, meat, air, feed, or through contact with infected animals, respectively. The transmission of rabies through dog bite (98.4%), need of post-exposure vaccination	It was concluded that there is a need to create awareness and improve knowledge of livestock farmers toward zoonotic diseases for its effective containment in Punjab.	moderate

							(96.8%), and annual vaccination of dogs (78%). About 69.2% respondents belonged to low to medium knowledge level categories, whereas 30.8% respondents had high knowledge ($p<0.05$) regarding different aspects of zoonotic diseases		
2	Zaidi et al., 2013	Geographic Variation in Access to Dog-Bite Care in Pakistan and Risk of Dog-Bite Exposure in Karachi: Prospective Surveillance Using a Low-Cost Mobile Phone System	The aims of this study were to: 1) estimate the burden of dog bites in Pakistan; and identify high risk neighborhoods for dog-bite exposure in Karachi, Pakistan's most populous city. .	Prospective surveillance	6212	Spatial analysis with odd ratios	The study shows a total of 6212 dog-bite cases were identified over two years starting in February 2009 with largest number reported from Karachi (59.7%), followed by Peshawar (13.1%) and Hyderabad (11.4%). Forty percent of patients had Category I (least severe) bites, 28.1% had Category II bites and 31.9% had Category III (most severe bites). Patients visiting a large public hospital ER in Karachi were least likely to seek immediate healthcare at non-medical facilities (Odds Ratio = 0.20, 95% CI 0.17–0.23, p-value,0.01), Spatial analysis of dog-bites in Karachi suggested clustering of cases (Moran's I = 0.02, p value,0.01), and increased risk of exposure in some areas The direct cost of operating the mHealth surveillance system was USD 7.15 per dog-bite case reported or approximately USD 44,408 over two years.	It was concluded that significant differences exist in access to care in Pakistan following dog-bites. It was further concluded that mobile phone technologies for health (mHealth) allowed for the operation of a national level disease reporting.	Strong
3	Dey et al., 2011	Human rabies among the paediatric population in Bangladesh	To see the patterns of presentation, age group at risk, state of vaccination following animal exposure and the interval between animal exposure and the development of the disease.	Crossectional study	70	SPSS version 16	Findings of the study showed 94.3% patients presented with bleeding from the site of injury and 4(5.7%) were without bleeding. Among the patients 53(75.7%) presented with bite on the limbs followed by bite on the face 8(11.4%), body 5(7.1%) and head 4(5.7%) cases. Thirty nine of the cases (55.7%) presented with multiple bites and 31(44.3%) had single bite. More than half that is 37(52.9%) patients presented with severe bite, 31(44.3%) had moderate bite and only 2(2.9 %) patients presented with mild bite. Fifty nine (84.3%) patients were unvaccinated whereas 11(15.7%) had history of vaccination after bite. Fifty two (74.3%) gave the history of bite by stray animal, 10(14.3%) by known rabid animal whereas 8(11.4%) had the history of bite by pet animal.	It was concluded that the 5-10 years group children were affected most, bites were mostly by stray animal, most of the children did not get post exposure prophylaxis and incubation period was between 11 to 150 days	moderate
4	Joseph et al., 2014	Determinants of delay in initiating post-exposure prophylaxis for rabies prevention among animal bite cases: Hospital based study	To study the factors associated with delay in initiation of PEP among animal bite cases attending anti-rabies clinic in the out-patient department (OPD) of a hospital in Delhi.	Crossectional study	200	SPSS version 17 and Chi-square test	The findings indicated delay in initiation (vaccine initiation in more than or equal to 48h) of PEP was found among 41% of the studied subjects. The mean time spent during each visit by the study subjects were 3.46h (SD1.60). Delay was more likely in people living at a distance of more than 10kmfromthevaccinationcentre ($p < 0.001$) and with a monthly family income less than 5000INR($p = 0.004$).	The study concluded that accessibility and lower economic status were the major factors associated with delay in initiation of PEP for rabies prevention.	Strong

							Delay showed an increasing trend with age (p = 0.041). Most commonly cited reasons by the respondents (n=82) for the inability to come early for vaccination included work related barriers(42.68%),anti-rabies clinic being closed on Sundays/national holidays (36.59%)and unawareness about timely PEP (31.71%).		
5	Sharma et al., 2016	Prevalence of Dog Bites in Rural and Urban Slums of Delhi: A Community-based Study	The aim of this study is to determine the prevalence of dog bites and its management in North West Delhi, India	Crossectional survey	2887	Chi square analysis	The study findings indicated dog bite incidence rate for the study population for the last year as 25.2/1000 population with higher rates in urban (30.1/1000) than rural (19.6/1000) slum. It was further identified that about half of the dog bite patients did not wash the wound with soap and water. The practice of washing the wound with soap and water was significantly higher in urban than rural slum. A majority (79.0%) of the patients did not receive anti-rabies serum.	The study concluded poor knowledge and dog bite management practices is a worrisome trend which policy makers should take into account to make India rabies free.	Strong
6	Ghosh et al., 2016	Awareness of rabies and response to dog bites in a Bangladesh community	to explore people's awareness about rabies, their attitudes towards dogs and practices associated with treating dog bites in Satkhira Sadar, a southwestern sub-district of Bangladesh.	Crossectional survey	3200	Odd ratios	The findings reported majority of the respondents who have heard about rabies (73%) and high level of awareness that dog bite is the main cause of rabies (86%), and that rabies can be prevented by vaccination (85%). 59% of the dog bite victims first seek treatment from traditional healers instead of visiting the hospitals, 29% received the rabies vaccine, 2% practiced proper wound washing with soap and water. Of the respondents, 5.2% reported a history of dog bite in at least one family member, and 11.8% reported a history of dog bite in domestic animals during the previous year. As a measure for dog population management (DPM), 56% preferred sterilization while the rest preferred killing of dogs.	It was concluded that treatment seeking behaviours of the respondents should be improved through additional education and awareness programme and better availability for the provision of post-exposure prophylaxis in Bangladesh.	moderate
7	Wasay et al., 2012	Knowledge and attitudes about Tetanus and Rabies: A population-based survey from Karachi, Pakistan	To evaluate public knowledge regarding predisposing factors, fatality and prevention of Tetanus and Rabies and attitudes toward vaccination and post-exposure prophylaxis	Crossectional survey	1201	multivariate analysis	Findings of the study indicated majority of respondents with knowledge of rabies (n= 699; 58%). Only three (11%) of these dog bite victims received some kind of vaccine or post-exposure prophylaxis. The majority of the participants were not aware of the fatality of these diseases and the importance of vaccination and post-exposure prophylaxis. Of the total respondents, 563 (47%) reported an injury or wound during the preceeding one year. Of them, 426 (76%) received a Tetanus injection. Out of the total study population, 1019 (85%) respondents did not know that Tetanus could be a fatal disease, and 844 (70%) did not know that Tetanus could affect and kill newborns.	The study concluded that dog bites are a common occurrence in Karachi and most of the participants were not aware of the fatality of these diseases and the importance and affordability of vaccination in case of dog bites and minor trauma	Strong
8	Dodet, et al., 2008	Rabies awareness in eight Asian countries	This paper aimed at identifying the early	Multicentric and multi-country survey	4377	SAS software version 8.2	The study identified two major issues where active information of the population could make a difference.	This study concluded the critical need of	Strong

			management of bites before and after arrival at the rabies prevention centre				Firstly, the necessity to apply appropriate wound care and to consult the nearest rabies prevention centre as soon as possible. Secondly, children carry the main burden of rabies, hence, chools are underused as a source of information. Rabies information campaigns should target children as well as adults and, since most rabies victims are children, awareness campaigns in schools could be carried.	getting the government authorities of these countries interested and committed in reducing the mortality due to rabies.	

3.3 Findings of the study

3.3.1 Prevalence of human rabies

Three studies estimated prevalence of rabies infection in Pakistan, Bangladesh and India (Zaidi et al., 2013; Gosh et al., 2016; Sharma et al., 2016). Estimated prevalence of rabies infection in Pakistan according to the study of Zaidi et al., (2013) was 17,774 to 24,848 based on reports from 2 major tertiary health centres. These cases were only associated with dog bites and the estimate was from number of cases recorded and number of vaccines disposed from the facilities. Gosh et al., (2016) reported the prevalence of rabies infection with respect to estimated number of animal bites (200,000) and rabies deaths (2000) as of 2012. Sharma et al., (2016) on the other hand reported rates rather than exact number of cases in India. It was estimated that human rabies prevalence was 25.2 per 1000 persons in India (95%CI: 20-32/1000), with urban slum having more cases (30.1 per 1000, 95%CI: 22.5–40.6/1000) than rural slums (19.6/1000, 95%CI: 14.2–29.4/1000).

3.3.2 Animal bite/Exposure to Animals as a risk factor

Dog bite as a major risk factor of human rabies in south Asia is indicated in all the 8 included studies, with some of the dog bites having category 3 severities based on WHO classification (Hundai et al., 2016; Joseph et al., 2014). Similarly, dog bites were shown to affect more males than females in all the three countries (Hundai et al., 2016; Zaidi et al., 2013; Dey et al., 2011; Sharma et al., 2016). Over 90% of respondents in half of the studies (Zaidi et al., 2013; Dey et al., 2011; Joseph et al., 2014) reported dog bites as a risk factor for rabies infection, mainly through contact with saliva (Hundai et al., 2016) and a mean incubation period of 45.38 ± 26.91 days and the range was from 11 to 150 days (Dey et al., 2011). According to Sharma et al., (2016), proportion of respondents ever bitten by a dog was 68.5 per 1000 (95%CI: 56.6–82.6/1000) in Urban area of the study and 58.2 per 1000 (95%CI: 47.2–71.6/1000) in rural areas. Among the respondents studied by Ghosh et al., (2016), 5% had dog bite in at least one of their family members, out of which 3.6% had died of rabies infection in the year preceding the study. A multivariate analysis by Gosh et al., (2016) indicated that risk of dog bites were associated with having a pet dog (OR: 2.1, 95% CI: 1.4–3.2), caring/feeding community dogs (OR: 2.1, 95% CI: 1.4–2.9) and household size (OR: 1.13, 95% CI: 1.07–1.2). Similarly, Wasay et al., (2012) study indicated dog bites among its respondents as a major cause of rabies infection, whereby 2.5% reported dog bites on themselves and additional 18% on their family members. Of the respondents studied by Dodet et al., (2008), 84% had dog bites, out of which 23% indicated the dog bites in more than one family member.

Four studies reported exposure to other animal bite (apart from dog) or their product as a risk for contracting human rabies (Hundai et al., 2016; Joseph et al., 2014; Ghosh et al., 2016; Dodet et al., 2008). Hundai et al., (2016) reported exposure to livestock among famers as a source of the infection. It was revealed from the study

that over 50% of the farmers have handled animal placenta and abortion cases with their naked hand. Similarly, almost all the respondent engaged in milking and consuming unpasteurized animal product. Sleeping with animals might be another risk for rabies infection as indicated by the study (Hundai et al., 2016), although not statistically significant. Joseph et al., (2014) reported cases of rabies infection from monkey bite (4%) and a single case of rat bite (0.5%) and the remaining ones from dog bites. Dodet et al., (2008) study identified 12.5% of the respondents studied that were predisposed to rabies infection due to cat bites and/or scratches. Most of animal bites predisposing to rabies were indicated to be stray animals (Joseph et al., 2014; Ghosh et al., 2016).

3.3.3 Knowledge Factor

Five studies assessed knowledge as a factor affecting human rabies infection (Hundai et al., 2016; Sharma et al., 2016; Gosh et al., 2016; Joseph et al., 2014; Wasay et al., 2012). Hundai et al., (2016) study indicated that most of the respondents were not knowledgeable about zoonotic diseases. Only 30% of the respondents have sound knowledge of various aspects of zoonotic diseases including rabies. Three studies (Hundai et al., 2016; Sharma et al., 2016; Gosh et al., 2016) indicated sound knowledge of rabies prevention among the respondents but majority did not put the knowledge into practice. Accordingly, about half of the participants were aware of the mode of transmission of zoonotic diseases such as through meat, contaminated milk, air or direct contact with infected animals (Hundai et al., 2016). Of the respondents who have heard about the rabies infection, 82% were not aware of the need to immediately get vaccinated after dog bite to prevent rabies infection (Sharma et al., 2016). Similarly, Joseph et al., (2014) observed 36% of the respondents that are not aware of the need to seek for immediate treatment after exposure to animal bites. Additionally, more than half (52%) are not certain about the prognosis of animal bites, with 42% believing it is not curable (Joseph et al., 2014). Awareness about rabies is high among the respondents studied by Wasay et al., (2012), with 81% said to have heard about rabies infection. However, only 45% of them were aware of dog as a predisposing risk factor of rabies and only 16% knows rabies to be a fatal condition (Wasay et al., 2012). Similarly, Wasay et al., (2012) opined that knowledge of rabies/tetanus was found to be significantly associated with level of literacy and male gender using multivariate analysis

3.3.4 Traditional factor

Six studies identified traditional/cultural practices predisposing to rabies infection (Hundai et al., 2016; Zaidi et al., 2013; Sharma et al., 2016; Ghosh et al., 2016; Wasay et al., 2012; Dodet et al., 2008). Hundai et al., (2016) opined that over 30% of the respondents apply chilli powder after dog bite based on the misconception that hotness of the chilli can prevent them from contracting rabies infection. Similarly, according to Zaidi et al., (2013) study, about 53% of the respondents seek non-medical treatment immediately after dog bites, which eventually predisposed them to rabies infection. Looking at the geographical health seeking behavior of patients in Pakistan, it was identified that people from Hyderabad, Thatta, Abottabad, Manshera, Peshewar, Quetta and Bahawalpur were more likely to receive immediate care from non-medical means in comparison to their counterparts in the capital city of Karachi. However, this was closely associated with distance of healthcare centers.

Dodet et al., (2008) study in 8 Asian countries indicated 10% of the respondents who prefer traditional medicine than orthodox treatment. Similarly, Sharma et al., (2016) and Ghosh et al., (2016) respectively reported about 25% and 59% of subjects studied in India and Bangladesh, who indicated traditional medicine as more effective

in preventing/treating rabies infection. Furthermore, despite most of the respondents (65%) in Wasay et al., (2012) study agreed to go to the hospital whenever they experience dog bite in future, 7% are still of the opinion for adopting traditional/home remedies.

4.4.5 Socioeconomic factor

Only three studies explore socioeconomic related factors predisposing to rabies infection (Zaidi et al., 2013; Joseph et al., 2014; Dodet et al., 2008). According to Zaidi et al., (2013) study, patient from remote areas of Pakistan find it difficult to travel long distance for treatment of animal bite cases. For instance, some respondents indicated that they have to travel a distance of 120 minutes from Manshera to reach a health facility that gives anti-rabies treatment in comparison to victims from the capital city of Karachi, who need to travel only an average distance of 20minutes to reach health facilities (Zaidi et al., 2013). As a result of the distance of health facilities, 13 cases were reported dead during the study, 8 of which were from Manshera (Zaidi et al., 2013).Similarly, Joseph et al., (2014) reported long distance as a factor influencing development of rabies infection among dog bite victims in India. It has been estimated that patients have to travel an average of 3.46 hours to reach a health facility for anti-rabies vaccine, which is financially unaffordable to many of the affected persons. The study further reported that more than 100 Indian rupees is required to get a single anti-rabies vaccine, which significant number of the respondents could not afford. Furthermore, Joseph et al., (2014) observed delay in seeking for anti-rabies treatment due to low socioeconomic status, with respect to income of less than 5000 Indian rupees per month (p0.004), age of respondents (p0.041) and distance of more than 10km ($p<0.001$). Similarly, Dodet et al., (2008) identified 17% of the respondents who have to travel 3 days or more to reach a designated health facility and 6% need to travel for more than a week, hence discourages them from seeking for anti-rabies treatment following animal bite.

4.4.6 Poor Prevention Practice as a risk factor

Five studies investigated into human rabies preventive practices in the study areas (Hundai et al., 2016; Sharma et al., 2016; Dodet et al., 2008; Dey et al., 2011; Joseph et al., 2014). Best means of preventing rabies infection was by immediate washing with soap and water as reported by more than half of respondents in three studies (Hundai et al., 2016; Sharma et al., 2016; Dodet et al., 2008), although most of the patients did not practice that measure, which eventually predisposed them to the infection (Sharma et al., 2016; Dodet et al., 2008).

Joseph et al., (2014) observed that 56% of animal bite cases that attend anti-rabies clinic overcome rabies infection within 24hours of the bite. On the other hand, delay of more than 48 hours in seeking for treatment as observed in 41% of the respondents is characterized by progression of the infection. Hundai et al., (2016) study showed most respondents (78%) to be aware of vaccination of dogs which is done yearly in Punjabi and over 90% are aware of post-exposure vaccination. However, only around 50% of those affected by rabies infection underwent vaccination after the exposure; hence knowledge does not coincide with practice (Hundai et al., 2016). Similarly, other evidences indicate significant number of the respondents that fail to use anti-rabies vaccine or serum immediately after dog bite (Dey et al., 2011; Sharma et al., 2016). According to Dey et al., 2011 study in Bangladesh, only 16% of dog bite cases were vaccinated for rabies against 84% who remained unvaccinated. Sharma et al., (2016) on the other hand in India reported about 20% and 71% of the dog bite cases that did not use anti-rabies vaccine and anti-rabies serum respectively. Dodet et al., (2008) opined that those with category III dog bites need a combination of both vaccine and immunoglobulin for effective prevention of rabies

infection. However, only 22% of the respondents studied by Dodet et al., (2008), who had category III dog bite have received the recommended treatment.

DISCUSSION

The aim of this study is to examine the risk factors predisposing people to human rabies infection in south Asia, with a focus on data from Bangladesh, Pakistan and India. Current evidence available in this subject area examines individual risk factors and concentrates more on the major risk i.e. dog bite. This left the misconception among many that only dog bite can leads to development of rabies infection. This review study will therefore fill in this gap by exploring all the risk factors peculiar to south Asian countries with highest burden of rabies infection (Bangladesh, India and Pakistan). Eight (8) primary studies provided evidence for this study, all of which have moderate to strong methodological qualities based on the Checklist by Kennelly, 2011. However, heterogeneity in reporting findings from the included studies affected the presentation of results of this study, therefore a number of findings of this study were reported individually rather than in comparison.

Analysis of findings of this study indicates that risk of developing human rabies infection in south Asia could be associated with five major factors; the first and the most crucial is animal bite mostly from certain stray animals which include dog bite, cat bite or scratches, monkey bite, rat bite, and direct contact with these animals products. The second factor is associated with poor knowledge/awareness about human rabies or how it develops. Thus, people were ignorant of the need to seek for immediate treatment following animal bite in order to prevent development of rabies infection. The third factor is related to poor traditional or cultural practices of people following bites from the aforementioned animals. These practices complicates wound sustain from the animal bites and eventually leads to infection. The fourth factor is the socioeconomic reasons which can leads to development of the infection even if the other factors were in good shape. The last factor is related to inadequate use of preventive measures by the study respondents. Therefore, the high prevalence of the infection in these three south Asian countries (India, Pakistan and Bangladesh) is associated with one or more of the five broad identified factors above. For instance, Zaidi et al., (2013) reported as high as 24,848 based on reports from 2 major tertiary health centers only in Karachi and were only associated with dog bites and the estimate was from number of cases recorded and number of vaccines disposed from the facilities. This indicates that if data is available for the whole country, the prevalence of rabies infection could be a multiple of this figure and it would be worse if other animal bites form part of the data. In Bangladesh, the report by Gosh et al., (2016) indicated a much bigger prevalence, estimated at 200,000 in the whole country. The report in India on the other hand indicate a value as high as 25.2 in every 1000 persons, which can be estimated to affect about 2.5% of the entire population.

The finding of this study indicated dog bite as a major risk factor of human rabies in south Asia. This can be testified with the fact that dog bite among the respondents range from as high as 96% in two studies (Zaidi et al., 2013; Joseph et al., (2014) to as low as 5% in one study (Ghosh et al., 2016). The risk of dog bite is largely associated with having a pet dog, caring/feeding community dogs and household size as indicated in multivariate analysis by Gosh et al., 2016. This finding is in line with the studies of Morgan, (2007) and Knobel et al., (2005) in Europe and Africa respectively, who associated dog ownership with increased risk of dog bite. Most of the dog bites identified in this study are said to be at category 3 severities based on WHO classification (Hundai et al., 2016; Joseph et al., 2014). Other animal bites identified in the findings of this study include; cat, monkey and

rat. Exposure to these animals particularly by famers is associated with development of the infection (Hundai et al., (2016). Even though, only one case of rat bite was identified (Joseph et al., (2014), the risk of developing the infection was indicated to be significant. On the other hand, risk of cat bites was identified by Dodet et al., (2008), whereby 12.5% of the respondents were predisposed to rabies infection due to cat bites and/or scratches. Another finding related to animals is exposure to their body product. It was revealed from the study that over 50% of farmers who handled animal placenta and abortion cases with their naked hand are at greater risk of developing the infection (Hundai et al., 2016). This is in line with the findings of Eng and Fishbein (1990) in United State, who studied 183 cats and 113 dogs to examine the risk of rabies infection. The study identified that greater proportion of bites and human rabies was associated with rabid cats than rabid dogs. The findings are also supported by the study of Swanepoel et al., (1993) about rabies in southern Africa. The study shows that cases of rabies infection was found in various African countries from animals other than dogs, which include Bats and fox in Namibia, Cattle and jackals in Botswana and Zimbabwe, fox in Northern Cape Province, Bats and rodents in South Africa and cats in Bulawayo. Similarly, bats were identified to harbour the virus in some parts of North America, South America, Europe and Australia.

The finding of this study further indicates poor knowledge/awareness as a predisposing factor to human rabies infection. Many of the studies indicated most of the respondents with poor knowledge about zoonotic diseases including rabies. For instance, only 30% of the respondents studied by Hundai et al., (2016) have sound knowledge of human rabies. This is in line with many other studies like Franka et al., (2013), who established the fact that lack of educational outreach at the community levels has created a gap in knowledge as the most effective way of avoiding animal bites and the method of administering first aid following bites by infected animals. This may not be unconnected with the fact that the respondents who have heard about rabies infection, 82% were not aware of the need to immediately get vaccinated after dog bite to prevent rabies infection, and only 11% knows exactly about rabies vaccine (Sharma et al., 2016). Therefore increasing awareness levels is very important particularly at community level.

Another finding of this study reported poor cultural and traditional practices after animal bites which predisposed to development of rabies infection. It has been observed that rather than undertaking appropriate anti-rabies vaccine or immunoglobulin, a significant number of the respondents studied adopted using non-therapeutic measures. For instance, about 53% of respondents according to Zaidi et al., (2013) study seek non-therapeutic treatment immediately after dog bites, which eventually predisposed them to rabies infection. This is in line with the study of Cleaveland et al., (2002), who indicated a significant number of deaths from poor traditional practices following rabies infection in Tanzania. It was further identified that people from urban areas are more to seek for appropriate medical treatment than those of rural areas. This was depicted in the study of Hundai et al., (2016) in Pakistan, whereby respondents from rural areas of Hyderabad and Manshera among others are more likely to receive immediate care from traditional healers in comparison to their counterparts in urban areas, the capital city of Karachi.

Delay/failure in seeking for anti-rabies treatment is also associated with socioeconomic status of individuals. In India, it was reported by Joseph et al., (2014) that households with income less than 5000 Indian rupees in a month are less likely to use complete anti-rabies treatment due to its high cost. This is further confounded with the fact that people who reside in places far from the hospital find it difficult to bear the financial cost of

transporting themselves to designated health centres that provide anti-rabies treatment. For instance, a distance of more than 10km, 2 hours journey, and 24hour were respectively reported in India, Pakistan and Bangladesh which cost more than what the respondents can afford. Such people will therefore sought for an alternative means of treatment like using traditional methods identified above, leading to a number of complications (Joseph et al., 2014; Zaidi et al., 2013; Dodet et al., 2008). This is supported by the study of Cleaveland et al., (2002) and Knobel et al., (2005), who identified low socioeconomic status among respondents that cannot afford complete anti-rabies treatment in Africa and other parts of Asia respectively.

Finally, the finding of this study reported inadequate use of preventive measures as a factor contributing to the development of the infection. Prevention of rabies infection following animal bite is shown to be effective after receiving appropriate anti-rabies treatment within 24hours of the animal bite (Joseph et al., 2014). In contrast, delay of more than 48 hours in seeking for treatment is highly characterized by progression of the infection. The findings show that the initial response in preventing rabies infection was by immediate washing with soap and water as reported by more than half of respondents in three studies (Hundai et al., 2016; Sharma et al., 2016; Dodet et al., 2008), although most of the patients did not practice that measure (Sharma et al., 2016; Dodet et al., 2008). This can be associated with socio-cultural beliefs of the respondents, particularly those in rural areas, who prepare to apply their traditional preparations rather than washing with soap/water. Another finding related to preventive measure is vaccination of dogs which as indicated in one of the studies (Hundai et al., 2016). This is in line with the study of Abela-Ridder et al., (2016), who showed that prevention and control of canine rabies have been successful in north America, western Europe and a number of latin American countries through routine dog vaccination, responsible dog ownership and provision of life saving bites treatment. Similarly, many other evidences (Schneider et al., 2007; kasampimolporn et al., 2008; Davline and Vonvile, 2012) indicated effectiveness of dog vaccination as a preventive measure.

CONCLUSION

Based on these findings, it is concluded that most of the factors predisposing to rabies infection in the three south Asian countries (Bangladesh, India and Pakistan) are preventable, hence; Government authorities, non-governmental organizations and philanthropists should be more committed toward increasing awareness about the consequences of the infection as well as providing free and accessible treatments across each country.

DECLARATION

We declared that this submission is original, not under consideration by any other journal and no competing interests exist between the authors.

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