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Rabies meta-analysis in dogs and human

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ABSTRACT: Meta-analysis on rabies in India was done to estimate the prevalence of the disease in India. The data was obtained from the peer-reviewed articles and publications during 2010-2020. The data used in the present study includes the studies in which the samples were completely random. The Meta-analysis for the epidemiology and sero-prevalence of rabies was done on a total of 20 out of 32 selected studies. Further subgroup analysis was done for species, geographical regions, and diagnostic tests. The total sample size for prevalence estimation was 26605. Sero-prevalence of rabies in dogs showed non-significant Kendall's tau (0.4667, $p > 0.05$) and regression test revealed significant publication bias ($z = 0.3222$, $p > 0.05$). The majority of bite victims were between the ages up to 20 years (21.49%) followed by 20.30% in the ages between 21-40. In the studies that were mentioned, males were disproportionately more likely (71.87%) to have been bitten by a dog than females (28.13%). The majority of victims suffered animal bites on their extremities. Maximum dog bites were recorded in the evening (62.9%).

Key words: Age, female, male, meta-analysis, prevalence, rabies

Rabies poses a serious public health risk in underdeveloped nations, as shown by the fact that it claims the lives of more than 60,000 people annually, besides approximately 15 million people receive rabies post exposure prophylaxis (PEP) vaccines (Wilde *et al.*, 2016). The massive global efforts has been initiated to control the disease by launching public health awareness programmes in Asia and Africa, where canine rabies is enzootic and still accounts for more than 95% of fatalities (Thahaby *et al.*, 2020). The bite of a rabid dog kills roughly 20,000 people in India each year (Li, *et al.*, 2020). In India, rabies is an endemic disease. It is found in all of the country's states and union territories, with the exception of the Andaman and Nicobar Islands and the Lakshadweep Islands. India accounts for 35% of the global rabies burden (Hampson *et al.*, 2015). The incidence of rabies has remained stagnant and grossly under reported in India since a decade. There is a serious need to improve reporting systems to address the issue of lack of accurate data and its verification in a number of regions in the country to reflect true burden of the disease. Keeping this in view advantage of meta-analysis and considering the above facts of rabies infection as a public health concern the present research work was designed to know about epidemiology of Rabies.

MATERIALS AND METHODS

For the epidemiological analysis, a descriptive design was used after collecting the data analysis of all the studies

which were related to rabies for the past 10 years (2010-2020). The method for the collection was used computer search of literature and material search through non-electronic means like abstracts, thesis, journals, etc. Computer search for the literature was conducted from Science Direct, PubMed, Krishikosh, Google Scholar, ICAR-CeRA, Springer etc., on epidemiological and humanistic burden of dog bites and dog-mediated rabies. These data were entered into a Microsoft excel 2007 spread sheet for tabulation, analysis, ranking and other studies. In an excel spread sheet all the details like author, year of publication, sample size, diagnostic test and number of positive samples were included. State-wise subgroup analysis was carried out in Uttar Pradesh, Haryana, Punjab, Tamil Nadu, Andhra Pradesh, Kerala, Karnataka, Odisha, West Bengal, Rajasthan, Maharashtra, and Gujarat. The protocols used for the assessment of selected studies were Joanna Briggs Institute (JBI) and preferred reporting items for systematic review and meta-analysis protocols (PRISMA-Protocol). Forest plot (Hak *et al.*, 2016) was made and variance between the different studies was calculated by the method of Der-Simonian and Laird and the value that we get is known as tau square which is the total amount of true heterogeneity present on an absolute scale (Borenstein, *et al.*, 2010).

RESULTS AND DISCUSSION

A total of 20 studies were included in this meta-analysis study (Table 1). The sample size of rabies in humans was

26605. The forest plot showed the proportion of positive rabies cases 65%, (95%CI, 40.0-86.0) in humans. A significant heterogeneity was noticed between the study of human rabies ($I^2 = 100\%$, $\tau^2 = 0.3198$, $p=0$). The result of the present study is in accordance with Belete *et al.* (2021). Researchers' hesitation to publish non-randomized results may be a factor contributing to high prevalence, in addition to the publishers' negligence.

Table 1: Meta-analysis of rabies in male and female humans in different states/union territories of India

Study	State/UT	Number of cases	Male affected	Female affected
1	Kerala	225	166	59
2	Karnataka	495	382	113
3	Gujarat	1109	856	253
4	Odisha	136	86	50
5	Maharashtra	256	184	72
6	Rajasthan	4062	3512	550
7	Dadra and Nagar Haveli	745	449	296
8	West Bengal	67	37	30
9	Tamil Nadu	289	174	115
10	Andhra Pradesh	27	14	13
11	New Delhi	183	117	66
12	Haryana	10287	8362	1925
13	Madhya Pradesh	389	244	145
14	Chhattisgarh	19	12	7
15	Chennai	256	180	76
16	Goa	17	13	4
17	Bihar	83	62	21
18	Himachal Pradesh	6772	4361	2411
19	Punjab	102	66	36
20	Jammu and Kashmir	1086	849	237
Total		26605	20126	6479

Male

Rank correlation test is not able to identify a significant relationship between sample size and effect size (Kendall's tau = 0.0947, $p>0.05$). Egger's regression test result showed a significant publication bias ($z = 2.3031$, $p<0.05$). In the rabies cases of human male, plot identifies study 6 as an outlier and which contributing to the heterogeneity. Results show that there are no influential studies for male in meta-analysis. Total number of articles included in the meta-analysis in males was 20. The sample size of rabies in males was 20126. The forest plot showed the proportion of positive rabies cases 71%, (95%CI, 65.0-75.0) in humans. A significant heterogeneity was noticed between the study of rabies in male ($I^2 = 98\%$, $\tau^2 = 0.0137$, $p<0.01$) as also explained by Peters *et al.* (2008) through contour-enhanced funnel plots which help to differentiate of bias (Lean *et al.*, 2009).

Female

Rank correlation test was not able to identify a significant relationship between sample size and effect size (Kendall's tau = 0.0105, $p>0.05$). Egger's regression test result showed a significant publication bias ($z = 2.1689$, $p<0.05$). In the human rabies cases the plot identifies study 6 as an outlier which contributing to the heterogeneity. Results showed that absence of influential studies for female in meta-analysis. The total number of articles included in the meta-analysis in females was 20. The sample size of rabies in females was 6479. The forest plot showed the proportion of positive rabies cases 30%, (95%CI, 25.0-36.0) and a significant heterogeneity ($I^2 = 98\%$, $\tau^2 = 0.0139$, $p<0.01$), similar to the observation of Li *et al.* (2020).

Age

The majority of bite victims were between the ages of up to 20 years (21.49%) followed by 21-40 years (20.30%). According to reports from other research conducted in India, children are more likely to be bitten by dogs and less willing to defend them. The study found that both owned and stray dog bites were most common in people between the ages of 11- 20 because they interact with dogs more often (Hemagiri *et al.*, 2012). Furthermore, according to four studies, there were 11.7% (Hemagiri *et al.*, 2012), 34.1% (Khan *et al.*, 2014), 11.3% (Thahaby *et al.*, 2020) and 22.4% (Ghosh and Pal, 2014) of all victims who were bite victims in the age group of 0 to 10 years, respectively. According to these researches, the most bites occurred in the age range of 10 to 40 years: 56.25%, 68.8%, 61.32%, and 46.27%, respectively. According to a different study, in rural areas of Goa (Vernekar and Desai, 2018), the incidence of dog bites was 1.03%, 8.66%, and 1.7% for people aged 0-5, 6-10, and 11-16 years, respectively.

Socio-economic status

According to a study at Bellary, Karnataka, in 2011, lower socioeconomic classes account for 87.3% of children who have been bitten by dogs and in Kashmir during 2020 50% of the victims have a monthly income of less than Rs. 10,000 (Thahaby *et al.*, 2020). However, a research carried out in Tamil Nadu's rural areas during 2013-14 revealed that 73.7% of the victims were living above the poverty line (Venkatesan *et al.*, 2014).

Occupation

According to the studies, the %age of students who were bitten by dogs ranged from 10% to 34.3% of all victims. According to two studies carried out in rural areas, as many as 41.5%-55.7% of the victims were employed as farmers, labourers, or in other field jobs (Venkatesan *et al.*, 2014). Unskilled workers account for 30.1% of all victims,

according to a study done in metropolitan hospital settings (Bourhy *et al.*, 2020).

Category of Rabies Exposure in Bites

According to the studies, dog bites for category II exposures ranged from 29.83% to 82%, while those for category III exposures ranged from 12.7% to 70.6% as also reported by Thahaby *et al.* (2020).

Site of Wounds

The majority of victims suffer animal bites on their extremities. Some researches revealed the locations of the wounds, 55.03% to 83.2% of the victims in these studies had lower limb, gluteal, and genital bites, whereas only 1% to 13.4% of all wounds in these studies were to the head, neck, and face in agreement with Ghosh and Pal (2014).

Number of wounds

The number of wounds per encounter was only reported in two studies. In a community-based study, 80% of victims reported only one wound (Hemagiri *et al.*, 2012), compared to 58% of all children under the age of 15 who sustained 2-4 wounds (Venkatesan *et al.*, 2014).

Time of bite

Maximum dog bites were recorded in the evening (62.9%) in the cross-sectional study done in Srinagar, whereas maximum (82.3%) dog bites were recorded in the morning in the study done in rural Maharashtra (Wankhede *et al.*, 2013).

Type of biting dog

Five of the studies reported that stray dog as the biting animal in 97.2%, 96.48%, 92.8%, 80.99% and 61.1% of the total cases in the respective. According to the prospective cohort study from Shimla, pet dogs were responsible for 57.1% of all dog bites, with unvaccinated stray dogs kept as pets accounting for 26% of all pet dogs. Of the total dog bites, stray dogs were responsible for 42.9 %, including 270 potentially rabid dogs and 26 lab-confirmed rabid dogs (Bharti *et al.*, 2019). According to a modelling study released in 2015, there is a 0.545% chance that the dogs that bite are rabid (Masthi and Sudarshan, 2015).

Vaccination status of the biting dog

In the above study the vaccination status of the biting dogs was only recorded in 3 investigations and in two studies, 52 % of all total dog bite cases lacked information on the dog's immunisation history. In addition, only 8.1%, 11% and 33.6% (Sharma *et al.*, 2022) of the instances involved

vaccination of the dogs.

Type of bite

According to two researches, the bite was unprovoked in 81.7 % and 100% of instances, but according to another study, the bite was unprovoked in just 55.5 % of cases (Vernekar and Desai, 2018).

CONCLUSION

In this study, the epidemiological humanistic burden, risk factors and diagnostic test of rabies in India was estimated. It has brought attention to the illness burden at the local, regional, and national levels, as documented in a variety of primary investigations, secondary data analysis, and modelling studies. Meta-analysis on the prevalence and sero-prevalence of rabies in humans and dogs revealed the pooled prevalence using random-effect model for rabies in humans was estimated 65% (95%CI: 40%-86%) and Pooled prevalence using random-effect model for rabies in humans was estimated in male 71% (95%CI, 65%-75%) and in female 30% (95%, CI: 25%-36%). The majority of bite victims were between the ages of 0-20 years (21.49%) followed by 21-40 years (20.30%). In the studies that were mentioned, males were disproportionately more likely (71.87%) to have been bitten by a dog than females (28.13%).

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