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Review Article

Probability of Concurrent Dengue and Malaria Infections: A Statistical Approach

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ABSTRACT

Malaria and dengue are public health challenges in most of Asian, African and South American countries. However, studies on concurrent infections with malaria and dengue are conspicuous by their scarcity. The present study utilizes the laws of probability to analyze the available data to highlight that co-infection with malaria and dengue is sufficiently frequent, and deserves higher level of suspicion by clinicians in geographical areas endemic to both infections.

Key words: Concurrent, Malaria, Dengue, Probability

INTRODUCTION

Despite a wide overlap between malaria and dengue-endemic areas, published reports of dengue-malaria co-infections are scarce in literature. The first patient with concurrent dengue and malaria (DM) was reported in July 2005. [(1)] Since then, few 'case reports' [(2-12)] have been published, indicating as if, the concurrent infections with malaria and dengue were a rarity. To an epidemiologist concurrence of two infections, one caused by a virus and other by a protozoan, both having distinct mean incubation periods, and transmitted by different vector mosquitoes with unique vector bionomics was interesting, and s/he was obviously keen to know the magnitude of the concurrence. One of the authors of this paper in his review article [(13)] proposed that the probability of concurrent infection can be arrived by using laws of probability. This paper attempts to calculate the magnitude of concurrence of DM using laws of probability, with an objective to highlighting the public health significance of concurrent infections.

MATERIALS AND METHODS

As mentioned above, concurrent dengue-malaria infection in medical literature has been dominantly presented as 'case reports', and number of epidemiological studies on the concurrence dengue and malaria are limited. The authors have used the results of available epidemiological studies, and recent epidemiological reports published by World

Health Organization to arrive at probability of concurrence of two infections.

a. Study A. Hundred and eleven microscopically positive cases of malaria (Pl vivax as well as Pl falciparum) aged 18 years and above, of both gender and residents of four regions of Brazilian Amazon, during the period 2003 to 2009 were tested for evidence of simultaneous dengue infection. Two of the 111 samples gave positive results, giving a concordance rate of 1.80%. [(14)]
b. Study B. In a retrospective study, out of 1,723 patients who consulted emergency department of Cayenne Hospital, French Guiana seeking treatment for symptoms suggestive of malaria and/or dengue during a one year period (July 2004–June 2005), 393 (22.8%) had smear-positive malaria (251 *P. vivax*, 133 *P. falciparum*, 2 *P. malariae*, and 7 mixed *P. vivax* and *P. falciparum).* Dengue was detected in 238 case-patients (13.8%). Concurrent dengue and malaria were confirmed in 17 of the 1,723 patients (0.99%), corresponding to 7.1% (17/238) of dengue cases and 4.32% (17/393) of malaria cases, respectively. [(15)]
c. Study C. A prospective study was conducted from August 2005 to December 2010 to document the nature and extent of concurrent dengue and malaria infections in Central Kolkata (India), an area endemic for both infections. Out of 2,971 patients clinically diagnosed as dengue fever, 605 (20.36%) had confirmed dengue infection. Forty-six of these were simultaneously suffering from malaria, a concordance rate of 7.60 percent. [(16)]
d. WHO Reports (D).

I. 50-100 million cases of dengue infections worldwide every year among 2.5 billion people at risk. [(17)]
II. World Health Organization has estimated that there were 216 million cases of malaria in 2010 in an 3.3 billion people at risk of malaria. [(18)]

RESULTS

Three studies A, B and C reveal that the concurrence rates of dengue-malaria infections as 1.80, 0.99 and 7.60 percents, respectively. However, it would be inappropriate to conclude that the probability of concurrent dengue-malaria infections lie in-between 0.01 and 0.076. The denominators in each study are different. In the study A the researchers detected two cases of dengue infections in 111 malaria positive cases; while in the study C the reciprocal was done i.e. the authors looked for Plasmodium infections in cases that were confirmed dengue cases.

In this regard, study B that detected the dengue and malaria co-infection in patients who reported to the hospital emergency department with clinical features of, either malaria or dengue or both is the most reliable for direct calculation of concordance rate. It also has a reasonable sample size (n=1723) that assures that the sample statistic would approximate population parameter. Using the data of study B, it can be shown that probability of concurrent dengue-malaria infection in patients with history suggestive of either or both is 0.0099 with 95% confidence limits as under:-

P (DM) = 0.0099 + 1.96 x 0.0024…… (V)

However, if we assume occurrence of malaria and dengue as two independent events, then using the same study B the figures of 393 and 238 cases of malaria and

dengue cases respectively out of 1723 clinical cases, the probability of concurrent DM infection in febrile patients clinically diagnosed as malaria or dengue should be

P (DM) = 93/1723 x 238/1723 = 0.031…….. (W)

With the same assumption, the probability of DM can also be arrived at by using WHO data (D). Occurrence of 50-100 million cases (say average 75) of dengue in 2.5 million population at risk, and 216 million malaria cases among 3.3 billion can be used for calculating the probability of dengue and malaria infection as:-

P (DM) = 75 million/ 2.5 billion x 216 million/ 3.3 billion = 0.0020…..(X)

The results of different studies can also be grouped to achieve our objective. Study A informs that the probability of *event* dengue, given that *event* malaria has already occurred is 2/111 = 0.0180, while Report D gives us P(M) as 216 million divided by 3.3 billion. Thus

P (D I M) = 0.0180 and P (M) = 216/3,300 = 0.0654

And P (DM) = P (M) x P (D I M) = 0.0654 x 0.0180 = 0.0012……. (Y)

Reciprocally, the study C gives us probability of malaria given that dengue has already occurred i.e. P (M I D) as 46/605, while WHO data gives the P (D) as 75 million/ 2.5 billion. Using the conditional probability

P (MD) = P (D) x P (M I D) = 75/ 2,500 x 46/ 605 = 0.0023…… (Z)

DISCUSSION

The availability of scarce medical literature on concurrent dengue and malaria infections give an impression that the concurrent rate is low to have clinical significance. However, the authors have used the available studies to arrive at probability of concurrent infections. The probability of concurrent dengue-malaria infections calculated indirectly (W to Z) varies from 0.0012 (Y) to 0.031 (W), with an arithmetic mean of 0.0091. Thus, on an average we should look for one case of concurrent dengue-malaria infection in every 100 cases of malaria or dengue in endemic geographical areas and during climatic conditions favourable to transmission of both infections. With 50-100 million cases of dengue and 149-274 million cases of malaria every year, the actual cases of concurrent infections would be staggering. Thus, there is a need for clinicians working in dengue and malaria endemic areas to be vigilant of the possibility of concurrent infections, especially in a case with atypical clinical presentation; unexpected laboratory reports (example thrombocytopenia in a case of malaria) or unsatisfactory response to treatment. High level of suspicion also needs to be exercised by physicians in malaria-dengue free regions when encountered with febrile patients with history of recent travel to a region endemic to both infections.

Indeed, the concurrent dengue and malaria infection seems to be an important clinical problem. The occurrence of this combination is higher than perceived by medical fraternity and evidenced by scarcity of literature on the subject. The present mathematical approach highlights the significance which also gets exalted by a recent study concluding that concurrent malaria-dengue infections have higher morbidity than either infection alone.[19]

Being a bio-statistical exercise, the limitations of the approach that may have influence on the results deserve mentioning. This study assumes that both diseases co-exist in space and time. Indeed, the vectors of malaria and dengue are not only different, but have unique vector bionomics. Concurrent infections can occur only if both vectors infected with respective pathogens interact with a host susceptible for both infections, within a limited time period. Of

interest, the vector for malaria has its main habitat in forest/ rural areas, while Aedes is more urbanized. Obviously, concurrent infection requires overlapping of geographical areas, and transmission period for two infections, or movement of susceptible host between two locations (say urban to rural/forested) in a limited time frame. It should also be appreciated that asymptomatic parasitemia is not uncommon in malaria endemic region, and will result in false positive report.

CONCLUSION

Multi-morbidity in non-communicable diseases and co-morbidity in TB-HIV have gained importance in clinical practice, public health and medical literature in recent decades. However, studies of concurrence in acute communicable diseases are glaring by their scarcity. This statistical approach attempts to bring concurrence rates of two acute infections on centre-stage for clinicians as well as public health authorities. This model can also be used to calculate concurrent rates of many other health related conditions, where direct evidence is lacking or difficult to arrive at. Obviously, results obtained through observational studies are more valid, but this model can be a starting point for initiation into less researched biomedical fields, and also assist calculation of sample size for prevalence studies when estimates are not available.

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