



## A Study on Dual Infections in Pyrexia Cases

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### ABSTRACT

*Co-existing infections (Malaria and dengue) go undetected due to lack of clinical suspicion and overlapping symptoms. Co-existing infections are on the rise in tropics. This study is undertaken to assess the prevalence of co-infections of some common tropical infections like malaria, dengue, typhoid, and leptospirosis in pyrexia cases. Also any associated complications with dual infections are dealt within this study. A cross-sectional study was undertaken including inpatient A.C.S. Medical college and hospital from May, 2013 to January, 2014 Suffering from fever of 100° and above with additional symptoms like Abdominal pain, Vomiting, Bleeding in both men and women between ages 5 and above and up to sixty years of age. A total of 100 pyrexia cases were studied. Of those 100 cases pyrexia, the percentage of a single infection, dual infection, triplet infection and other causes were 20%, 9%, 1% and 69% respectively. Among the dual infections, coinfection with malaria and dengue, dengue and typhoid, malaria and typhoid, dengue and leptospirosis were 33.33%, 22.22%, 22.22% and 22.22% respectively. One triplet infection with Malaria, leptospirosis and typhoid was also detected. There is prevalence of coexisting infections with tropical infections like malaria, dengue, leptospirosis and typhoid. Prompt detection of these dual infections can lead to decreased morbidity and mortality. A clinical suspicion must be present to detect these coexisting infections in pyrexia cases.*

**Keywords :** Co-infections, Dual Infections, Mixed Infections Iron Deficiency / Overload in Coinfections / Dengue / Malaria / Typhoid and Leptospirosis

### INTRODUCTION

#### *A Study on Dual Infections in Pyrexia Cases*

Co infection may be defined as, “ Concurrent infection of a cell or an organism with two organisms” [1]. The clinical manifestations of infections are myriad varying from life threatening process to brief and self-limited conditions to chronic conditions. Infectious agents undergo rapid evolutions and develop selective advantages that result in constant variations in the clinical manifestations of infections. Changes in the environment and host can predispose new populations to a particular infection. [2]. One of the clinical manifestations commonly encountered in most of the infections is pyrexia. Pyrexia is a host response due to release of cytokines like Interleukin 1, Tumor Necrosis Factor alpha and other factors associated with inflammatory and infectious responses[2]. Pyrexia is also a frequently encountered clinical manifestation in co-infections. Co infections may be associated with increased morbidity, mortality, and increased health care cost. Description of Co infections may help in primary, secondary and tertiary preventive care of patients with infections.

According to WHO, “Tropical diseases encompass all diseases that occur solely, or principally, in the tropics. In practice, the term is often taken to refer to infectious diseases that thrive in hot, humid conditions, such as malaria, leishmaniasis, schistosomiasis, onchocerciasis, lymphatic filariasis, Chagas disease, African trypanosomiasis, and dengue.”[3] WHO statistics show that malaria affected 207 million people and caused about 625,000 deaths [3]. The same statistics shows that deaths due to malaria in India are 2.40 per 100,000 population [3]. About 2.7 billion

people are at the risk of developing DENGUE infection [3]. It affects 50 -100 million people every year [3]. In South East Asia alone, 2.3 million people were affected in 2010 [3].

Extensive Research and Attention is being focused on newer emerging diseases like Human immunodeficiency virus (HIV) and Multiple Drug Resistant Tuberculosis (MDR-TB). Yet some existing infectious diseases like Malaria, TB remain a challenge for detections treatment and prevention in India.

Our study is on Co-existing infectious diseases which are now being increasingly noticed (E.g. Dengue and Malaria) [4] (Dengue and Typhoid etc.) [5] (Malaria and leptospirosis) [6], all occurring in the same patient simultaneously or within a span of ten days. These go undetected due to lack of suspicion and also due to overlapping of signs and symptoms.

Some of the existing co-infections occurring in India are Malaria and Dengue, Dengue and Typhoid, Tuberculosis and HIV infection [7], Hepatitis B virus and HIV infections [8], Hepatitis C and HIV infection [8]. These co-infections result in increased morbidity and mortality. The suspicion of dual infection is not high in today's clinical practice, which can lead to delayed diagnosis and treatment.

Co-infections were first described in the United States Army (Typhomalarial fever) [9]. Since there are no studies at present which address the prevalence of dual infections in India, this study was undertaken to find out how common are dual infections in patients with fever in India. The present project study aims at analysis of cofactors, myths and reasons, and occurrence of some common tropical infections like Malaria, Dengue, Leptospirosis and typhoid at A.C. S Medical College, Chennai.

#### **Aim and objectives of the project**

1. To study prevalence of coexisting enteric fever and malaria in the sample.
2. To study prevalence of coexisting Leptospiral and Dengue fever.
3. To arrive at any common coexisting factors for above infections.
4. To correct serum iron levels with occurrence of Enteric fever following malaria.
5. To suggest prevention and control measures for above infections.

#### **MATERIALS AND METHODS**

This study utilized prospective descriptive design. Ethical committee approval was obtained in ACSMCH. Verbal consent was obtained from the patients. The setting of the study included male and female medical wards (Inpatient) of ACSMCH.

A total of 100 pyrexia cases were studied from May 2013 – January 2014. Effort has been made to identify true co infections based on Relevant Laboratory Tests.

#### **Inclusion Criteria**

Inpatients of medical ward at ACS Medical College suffering from fever of 100° and above with additional symptoms such as abdominal pain, Vomiting, Bleeding, both men and women between ages 5 and above and up to sixty years, were included. .

#### **Exclusion Criteria**

- 1) Children below 5 years
- 2) Too cortically ill patients
- 3) Pyrexia cases with infections other than the above four diseases.

#### **Data collection**

Multiple data collection methods and sources were employed in the study. Data collection included questionnaire, biophysical data, demographic data and clinical data.

A structured questionnaire was developed and content expert validity obtained. It was utilized for interviewing patients consistently by a single data collector to maintain consistency and constancy within the study.

Biophysical data were collected utilizing diagnostic laboratory tests including ELISA method (Jai Mithra) for dengue diagnosis, Card test(Standard diagnosis)- (ELISA and Jai Mithra) for Leptospirosis, Staining and card test-Panbio (Standard diagnostics) for malaria diagnosis, Tube Widol test with confirmation by blood culture for Typhoid diagnosis, Kit Grainer diagnostic GmbH(Germany) for serum iron detection. Additional data like blood group, ECG, blood urea and creatinine and liver function test results were obtained.

Demographic data were collected through interview. Clinical data were collected utilizing patient charts. Data sources were questionnaire, patient charts, laboratory test report and ELISA.

Data were tabulated and analyzed utilizing descriptive statistics. Frequencies, averages and percentages were calculated.

## RESULTS AND DISCUSSION

A total of 100 pyrexia cases were studied. Of those 100 cases, pyrexia due to a single infection, dual infection, triplet infection and other causes were 20%, 9%, 1% and 69% respectively. Among the dual infections, coinfection with malaria and dengue, dengue and typhoid, malaria and typhoid, dengue and leptospirosis were 33.33%, 22.22%, 22.22% and 22.22% respectively. One triplet infection with Malaria, leptospirosis and typhoid was also detected.

**Table 1. Distribution of Infections and Pyrexia**

	Total
Pyrexial cases studies	100
Single infection	20
Dual infections	9
Triplet infections	1
Pyrexia of other causes	69

Of the 100 pyrexia cases studied, totally 10 cases of co infections were detected of which 9 cases were dual infections and 1 case was a triplet infection. Out of the 100 pyrexia cases studied, 30% of pyrexia was caused due to infection of which co infection contributed to 10% of cases and infection with a single pathogen contributed to 20% of cases. This shows that 1/3 of the pyrexia cases due to an infection has been due to co infections with two or three pathogens. So a diagnosis of a single infection must not stop the clinical suspicion of maybe a concurrent infection with another pathogen. This finding may help in diagnosis of the cause of pyrexia as co infection with two or three pathogens rather than a single pathogen. Future studies should focus on early diagnostic methods of co infections which would help in early diagnosis and treatment.

**Table 2. Single Infection (Tropical Disease in Study – Malaria, Dengue, Leptospirosis, Typhoid)**

Infection	Males	Females
Dengue	8	4
Malaria	2	2
Leptospirosis	0	0
Typhoid	3	1
Total	13	7

**Table 3: Distribution of Dual Infections**

Dual infections	Males	Females
Malaria + Dengue	3	0
Dengue + Typhoid	2	0
Malaria + Typhoid	1	1
Dengue + Leptospirosis	2	0
Total	8	1

Dengue, malaria, leptospirosis and typhoid were the four tropical diseases included in this study. Infection with a single pathogen was found in 20% of the cases. Among 100 cases, Dengue infection was commonly found in most number of cases accounting for 12%, whereas malaria and typhoid found in 4% each. Of the study population, leptospirosis was not detected in any of the cases. Of the 20 cases of single infection, male sample contributed to 65% among single infection. In this study population, Dengue and malaria contribute to 16 cases in total out of the

20 cases of single infections. This shows that vector borne diseases are more prevalent in a developing, tropical country like India among the cases included. So this finding may help in improving the primary prevention methods including patient's education like prevention of water logging and secondary prevention of vector borne diseases.

A total of 10 of cases were co infections. Among the coinfection cases, 90 % was dual infections with two pathogens. Of the 9 cases of dual infection, Malaria and dengue infections were found in 33.33 % of cases, dengue and typhoid, dengue and leptospirosis and malaria and typhoid contributed to 22.22% of cases respectively. Of 9 cases of dual infection, the distribution indicates that 88.88% of dual infections were prevalent among the male sample. This may show a warrant a gender predilection of dual infections. This finding has to be further explored in future studies. From this finding co infection with malaria and dengue is most common among the cases. Both being vector borne diseases, which are caused by environmental factors and vector, emphasize the role of environment in the disease process. Further, the co-existence of typhoid infection with malaria and dengue indicates the impact of environmental interventions in primary prevention of tropical diseases. Future research may focus on a rapid, focused diagnostic test to detect both malaria parasite and the dengue virus.

**Table 4: Distribution of Triplet Infections**

Triplet infections	Males	Females
Malaria + Leptospirosis + Typhoid	0	1
	0	1

A single case of triplet infection with malaria, typhoid and leptospirosis was found in a female of the 10 coinfection cases. This finding has to be further explored with a large sample size in future studies.

**Table 5: Thrombocytopenia Complication in Single Infection vs. Dual Infections**

Thrombocytopenia	Males	Females	Total
Single infection	4	0	4
Dual infections	4	0	4

Thrombocytopenia is common in viral infections like dengue. When thrombocytopenia was compared in single infection and dual infection cases, all 4 cases with thrombocytopenia were found in single infection cases.

**Table 6: Anemia in Single Infection vs. Dual Infections**

Anemia	Males	Female	Total
Single infection	1	1	2
Dual infections	0	1	1

Iron deficiency anemia is a common finding among tropical infections. Of the 30 cases of infections in this sample, 26.66% cases had anemia. When a comparison was drawn between the distribution of iron deficiency anemia among single infection and dual infections, 4 cases with iron deficiency anemia were found in each.

## CONCLUSION

There is prevalence of coexisting infections with tropical infections like malaria, dengue, leptospirosis and typhoid. Prompt detection of these dual infections can lead to decreased morbidity and mortality. A clinical suspicion must be present to detect these coexisting infections in pyrexia cases. This can lead to prompt diagnosis and management of these co-infections. Also, emphasis primary prevention of these tropical infections in India will decrease the morbidity and mortality from these infections.

### Appendix:

#### Study of Dual infections in pyrexia cases:

#### Patient details questionnaire:

1. Name:
2. Age:
3. Sex:
4. Address:
5. Rural/Urban/floating population:

6. Diet : Veg or Non-veg/ Home food or eating outside:
7. Housing (surroundings) – Hut, small houses, flat, individual houses. Water body around the houses.
8. Number of family members:
9. Number of children < 15years:
  - If female :

Menstrual disorders (Hb%, blood group etc.,)

10. Occupation:
11. Language spoken:
12. Personal history:
  - Smoker – Tobacco, cigarette
  - Alcoholic/drugs
13. Use of water – drinking

Ordinary well/ bore well/ tap water/ boiled water

14. Past history of illness or fever E.g.: malarial typhoid etc.,
15. In women leading to arrive at increased blood loss like :
  - Increased menstrual loss,
  - No. of deliveries or abortion.
  - Iron taken so far
  - History of blood transfusion if any.
16. Anti-mosquito measures used: Mosquito net/insecticides (around home)/ mosquito coil (chemical or herbal)/ Mosquito oil like goodnight.
17. How often water is chlorinated (of wells)
18. Any Typhoid or malarial vaccinations taken so far.
19. History of hospitalization so far/ for what purpose.
20. History of steroid/ any drugs for hypertension and diabetes mellitus used for any other illness.
21. Any water body around the house:
22. History of travel to malarial endemic areas:
23. History of food intake outside and how often:
24. History of protein in diet:
25. Any immune-suppressed state: Diabetes mellitus/hypertension/HIV/ stent/organ replacement.

#### **Other data:**

1. HB % :
2. Blood group :
3. Platelet count :
4. Serum creatinine :
5. Blood urea :
6. History of jaundice :
7. History of blood transfusion :
8. Diagnosis :
9. Treatment :
10. Outcome :

#### **REFERENCES**

- [1] Merriam-Webster. Coinfection. 11-30-2014]; Available from: <http://www.merriam-webster.com/dictionary/coinfection>
- [2] Fauci, B., Kasper, Hauser, Longo, Jameson, Loscalzo, ed. Harrison's Principles of Internal Medicine. 17th ed ed. 2008, McGraw Hill Companies, Inc.: United States of America.
- [3] World Health Organization. Tropical Diseases. Retrieved from: [http://www.who.int/topics/tropical\\_diseases/en/](http://www.who.int/topics/tropical_diseases/en/)
- [4] Carme, B., Matheus, S., Donutil, G., Raulin, O., Nacher, M., & Morvan, J. (2009). Concurrent Dengue and Malaria in Cayenne Hospital, French Guiana. *Emerging Infectious Diseases*, 15(4), 668–671. doi:10.3201/eid1504.080891

- [5] Uneke, C. J. (2008). Concurrent malaria and typhoid fever in the tropics: the diagnostic challenges and public health implications. *Journal of vector borne diseases*, 45(2), 133.
- [6] Wongsrichanalai, C., Murray, C. K., Gray, M., Miller, R. S., McDaniel, P., Liao, W. J., ... & Magill, A. J. (2003). Co-infection with malaria and leptospirosis. *The American journal of tropical medicine and hygiene*, 68(5), 583-585.
- [7] Sharma, S. K., Mohan, A., & Kadiravan, T. (2005). HIV-TB co-infection: epidemiology, diagnosis & management. *Indian Journal of Medical Research*, 121(4), 550-567.
- [8] Saravanan, S., Velu, V., Kumarasamy, N., Nandakumar, S., Murugavel, K. G., Balakrishnan, P. & Thyagarajan, S. P. (2007). Coinfection of hepatitis B and hepatitis C virus in HIV-infected patients in south India. *World Journal of Gastroenterology*, 13(37), 5015.
- [9] Smith DC (1982a). The rise and fall of typhomalarial fever. I: origins. *J.Hist. Med. Allied Sci.*, 37: 182-220.