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Autopsy findings in Acute febrile illness (AFI) in a tertiary health care centre - one year study.

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Abstract

Background: Acute febrile illness has a diverse pathogenesis, with variable morbidity and mortality in developing countries. The objective of this study is to find out the etiology and histopathological findings of fatal febrile illness as found at autopsy.

Design: A total 600 autopsies were performed from Jan 2019 to Dec 2019. Out of these in 75 cases there was a history of fever of variable duration. 46 cases fulfilled criteria of acute febrile illness. Clinical details, investigations details were collected from medical records. Microscopic findings were recorded.

Result: Out of total 46 adult autopsies, there was intrapulmonary haemorrhage with oedema in 23 cases, 10 cases with acute respiratory distress syndrome (ARDS), 7 cases with pneumonia, 8 with dengue,3 cases each of leptospirosis and septicaemia, 6 cases with pyelonephritis, 2 of Tuberculosis & one case each of malaria, giant cell pneumonitis, & typhoid.

Discussion: Acute febrile illness is a presentation caused by different etiological factors. It is characterized by sudden onset of fever without apparent localized site or cause of infection, less than 7 days, may be associated with breathlessness, body ache, headache, weakness. Some patients had vomiting, haematuria, Haemoptysis as well.

Conclusion: The predominant finding in fatal AFI was intrapulmonary haemorrhage, oedema, and ARDS on gross as well on microscopy. Fever, a common presentation, requires prompt diagnosis and appropriate timely management to prevent this and other fatal complications. The study also reaffirms the utility of post mortems in an era when it is fading rapidly.

Keywords: acute febrile illness, autopsy findings, ARDS, intrapulmonary haemorrhage.

Introduction

There has been a rapid emergence and re-emergence of viruses, bacteria and parasitic infections, including new pathogens as well as those previously believed to be under control during the past two decades. Many of these pathogens cause acute undifferentiated febrile illness (AUFI), or acute febrile illness (AFI). Acute onset of fever, chills, myalgia, and fatigue are common features of many infections that are endemic in India. In many areas in developing countries diagnostic facilities are limited due to which etiology of acute febrile illness (AFI) remains largely unknown. Criteria for Acute febrile illness is sudden onset of fever without apparent localized site or cause of infection, less than 7 days, may be associated with breath lessness, body ache, headache, weakness. Physicians often diagnose patients mainly based on clinical features and knowledge regarding circulating pathogens. The common causes of AFI include malaria, dengue fever, enteric fever, leptospirasis, rickettsiosis, hantavirus and Japanese encephalitis. [1–3] AFI contributes to substantial morbidity and death among children and adults worldwide. [4,5] During monsoon season, dengue fever and malaria are endemic in many parts of India. Leptospirosis and scrub typhus are zoonotic infections which are widely prevalent in areas with heavy monsoon.

Many preventable deaths occur because of incorrect or delayed diagnosis, mainly due to limited access to medical care and laboratory diagnostic facilities in the developing countries [6–9] and the clinical presentation with non-specific symptoms such as low-grade fever, general malaise, headache, arthralgia, myalgia, and rash. Accurate clinical diagnosis is difficult without laboratory confirmation. [10–12] Evidence-based decision-making in health requires the availability of sound data, but good quality information on the occurrence of infectious diseases is unavailable for most countries in Asia. [13] Understanding the common causes of AUFI in resource-poor settings in tropical and subtropical countries will help improve case management. Autopsy is helpful in cases where antemortem diagnosis is not possible and in brought dead patients.

Although autopsy is one of the most important tools of quality assurance in critical care medicine, postmortem examination rates have continued to decrease during recent years. [14,15] Detailed knowledge of postmortem findings in these patients could not only improve our understanding and treatment of AFI, but also provide direction for future research strategies. In this context, we conducted a retrospective observational study to investigate the cause of death and histopathological findings among AFI cases.

Materials and methods

A retrospective observational study was carried over a period of one year from January 1, 2019, to December 31, 2019 at our tertiary health care centre in Mumbai. All adult autopsies conducted by department of patho logy with age more than or equal to 18 years and ful filling the criteria of acute febrile illness were included in the study. Cases having history of sudden onset of fever more than 38.5 degree Celsius for more than 7-8 days was considered as acute febrile illness. Paediatric and maternal mortality cases were excluded from the study.

Autopsy records were studied, confidentiality was maintained and the identity of the individuals was not revealed at any point in the study. Clinical details such as age, gender, hospital stay duration, clinical symptoms with history, clinical diagnosis and reports of laboratory

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and radiological investigations were collected from medical records at the time of autopsy.

In each case, external as well as in-situ examination with dissection and examination of the visceral organs was done. Representative pathological sections were taken & placed in 10% neutral buffered formalin. Blood culture, blood investigations and culture of other tissue specimens was performed as per indication. A detailed gross examination of all the organs and histopathology of at least one representative section from each organ such as brain with meninges, heart, liver, spleen, kidney was carried out. Paraffin sections were then stained with routine Haematoxylin and Eosin. Special stains like Ziehl Neelsen, Periodic Acid Schiff were done whenever necessary. The autopsy findings were correlated with detailed clinical information and investigation in each case to establish the accurate cause of death.

Results

Total 600 adult autopsies were carried out at our institution during the period of 1st January 2019 to 31st December 2019. In a total of 75 autopsy cases there was history of fever of variable duration. Of these 46 fulfilled criteria of acute febrile illness. Most cases were in the younger age group (18–30 years) (Table 1), and the mean age was 38.93 ± 15.29 years. 40 (87.0%) were males and 6 (13%) were females with male to female ratio of 6.67.

Most common symptom among cases other than fever was chills (28 cases) followed by dyspnoea among 10 cases, cough in 7 cases, body ache and altered sensorium in 4 cases each and vomiting in 3 cases (Table 2). Most common autopsy finding was intrapulmonary haemorrhage seen in 23 cases followed by acute respiratory distress syndrome in 10 cases. (Table 3)

Table 1: Distribution of cases according age.

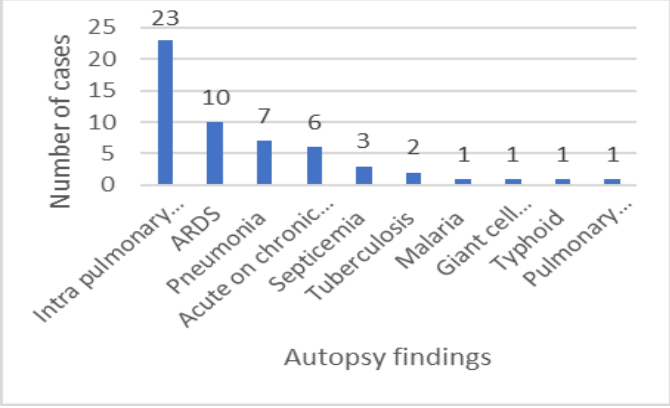
Age group (years)	Number of cases (N=46)	Percentage
< 20	6	13.04
21-30	14	30.44
31-40	10	21.74
41-50	6	13.04
>50	10	21.74

Mean age: 38.93 ± 15.29 years

Table 2: Distribution of cases according to presenting signs and symptoms.

Signs and symptoms	Number of cases (N=46)	Percentage
Fever	46	100
Chills	28	60.86
Dyspnoea	10	21.73
Cough	7	15.21
Body ache	4	8.6
Altered sensorium	4	8.6
Vomiting	3	6.5

Graph 3: Distribution of cases according to autopsy findings



Intrapulmonary haemorrhage was the commonest finding seen in 23 out of 46 cases. One case had dual infection (plasmodium vivax malaria & Dengue infection). Grossly the organs were boggy, voluminous

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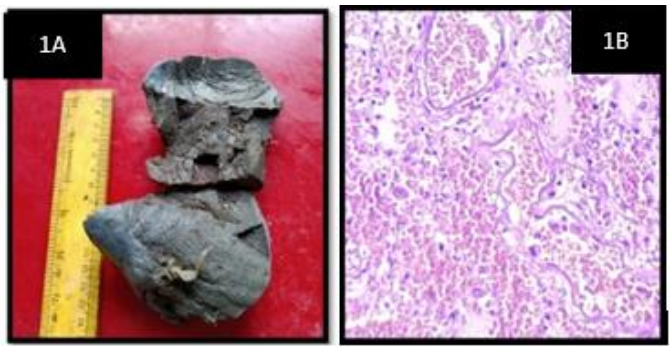
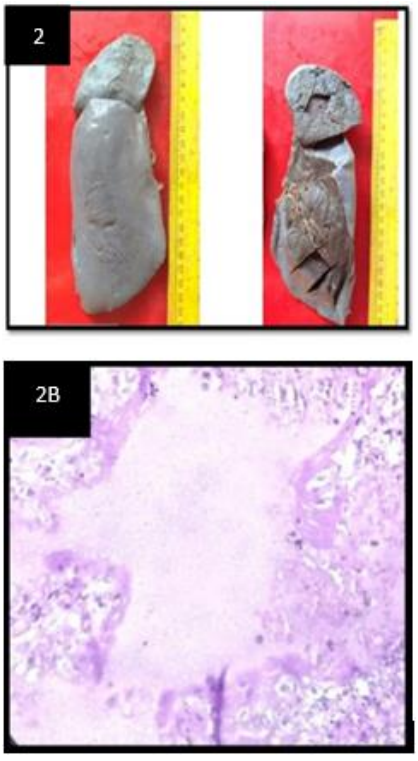
& blood oozed out on pressure suggestive of intra pulmonary haemorrhage (Figure 1A). On histo patho logy, lungs show thickened alveolar septae, alveolar spaces are filled with RBC (Figure 1B).

Figure 1:



In 10/23 cases, lungs were red angry looking on cut surface suggestive of acute respiratory distress syndrome (Figure 2 A). On histopathology of ARDS showed hyaline membrane formation on alveolar spaces (Figure 2B). there was interstitial and interalveolar oedema and collapsed alveoli.

Figure 2:



07 out of 46 cases showed features of broncho pneu monia. Giant cell pneumonitis and pulmonary throm bo embolism was seen in each case respectively. grossly lungs were markedly congested. Pleural and cut surface showed 1-4 mm greyish white lesion in lungs and on microscopy examination the bronchi were affected showing necrosis of bronchial epithelium and dense mixed inflammation consisting of neutrophils, lymphocytes, and congested capillaries. Two cases showed features of disseminated infection involving lungs, spleen, and kidneys on gross examination which were confirmed on microscopic examination showing caseous necrosis and epithelioid cell granulomas. One case of malaria showed slate grey like appearance on autopsy. On microscopic examination showed hemozoin pigment in liver & spleen. One case of enteric fever shows typhoid gastroenteritis.

Complete blood count was done in 31 out of 46 cases. Leukocytosis was seen in all 31 cases, neutrophilia in 28 cases, monocytosis in 16 cases and thrombocytopenia in 23 cases. Deranged liver function test was found in 8 out of 46 cases and deranged kidney function test in 6 out of 46 cases. Tests for Dengue and Leptospirosis were positive in 8 and 3 cases respectively. Widal test was positive (Titre 1:360) in one case.

Bilateral consolidation and infiltration suggestive of bronchopneumonia was seen on x-ray chest in one of the autopsy cases. On gross examination of lungs, more frequently bilateral lower lobe of lungs was affected showing multiple foci of consolidation.

3 cases with hepatosplenomegaly, pleural effusion and Choledo Cho lithiasis was detected on ultrasonography. CT findings suggestive of ground glass opacity, dense consolidation and bilateral lung infiltrate was seen in 3 cases. Urine routine microscopy was available in 2

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patients suggestive of 15-20 pus cell /HPF, 25-30 RBC/ HPF (occult blood positive) and culture sensitivity positive for MRSA. Postmortem investigation was done in 15 cases out of that one case was positive for malaria and dengue respectively.

Discussion

In tropical and subtropical South and Southeast Asian countries, the most common causes of AUFI were viruses, followed by bacteria and malaria. Generally, dengue fever was the commonest cause followed by leptospirosis and typhoid. [16]

In the present study, mean age of cases was 38.93 ± 15.29 years with male to female ratio of 6.67. Similar findings were seen in study done by Wangdi et al. [16] Males were more commonly affected than that of females. Fever was seen in all cases of AFI. Other symptoms presented were chills, dyspnoea, cough, altered sensorium, body ache and vomiting.

All the cases of dengue, leptospirosis and malaria presented with fever and chills. Cause of death was intra pulmonary hemorrhage in 1 case and acute renal failure in other 2 cases of leptospirosis. Pulmonary oedema was main cause of death in a case of dual infection with P. vivax and dengue. ARDS following gastroenteritis was the cause for mortality in one case of typhoid.

Autopsy of all cases of dengue in present study were having intrapulmonary haemorrhage. 1 case was reported in present study with dual infection of dengue and plasmodium vivax malaria which was diagnosed on postmortem investigations. Dengue is a systemic viral infection causing multiorgan pathology. Liver is the most commonly affected organ in Dengue Haemorrhagic Fever. [17] In dengue fever, acute liver failure predisposes to haemorrhage, DIC and encephalopathy which can be life threatening. These cases with liver pathology showed Haemorrhagic manifestations in other organs like gastrointestinal bleeding, intrapulmonary haemorrhage and intracerebral haemorrhage.

Lung involvement in Dengue fever is manifested as alveolar congestion, septal haemorrhages, diffuse alveolar haemorrhages and pleural effusions.

Clinically the patients with dengue Haemorrhagic fever can present as ARDS. The main lesion in kidney was Acute Tubular Necrosis (ATN) of proximal convoluted tubules caused by ischemia due to severe hypovolemic shock with significant blood loss [18].

3 cases were found to have septicaemia on autopsy. The main clinical and postmortem causes of death in critically ill patients succumbing to sepsis and septic shock is refractory multiple organ dysfunction syndrome and uncontrollable cardiovascular failure.

Relevant post mortem findings explaining these results were a continuous septic focus in 80% and cardiac pathologies in 50% of patients as mentioned by Torgerson et al [19].

In present study, the prevalence of ARDS was 21.74%. The prevalence calculated for ARDS in the study by Saha et al was 6.05%, while a similar study by Sachdev and Pandit had a prevalence of 3.15%. [20,21] This higher percentage may be explained because the present study was exclusively done on adult autopsies while the study by Sachdev and Pandit included both adult and Paediatric autopsies.[20]

The studies done by Estenssoro et al. and Singh et al. reported a prevalence of 6.8% and 7.4%, respectively. [22,23] present study reported higher prevalence of ARDS in autopsies as compared to other studies.

Present study reported 1 case of giant cell pneumonitis on autopsy findings. The classic pathologic findings are there of an interstitial pneumonia with prominent

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multinucleated giant cells lining alveolar spaces. These giant cells have typically distinctive intranuclear and/or intracytoplasmic eosinophilic viral inclusions. [24,25]

This is frequently accompanied by diffuse alveolar damage with hyaline membrane formation, reactive alveolar hyperplasia, necrotizing alveolitis, and proliferation of bronchial epithelium with squamous metaplasia. Typical giant cells are not always present and changes of secondary bacterial super infection may dominate the pathologic feature in some cases.

Conclusion

Intra pulmonary haemorrhage, oedema and acute respiratory distress syndrome are the complications leading to death in AFI.

Antemortem radiological and biochemical findings suggestive of the above indicate poor prognosis and reiterate the importance of acute & active management of AFI before these complications set in, to prevent fatality in preventable deaths. It also lays a focus on further need to presentation and eradication of these preventable diseases.

This can happen with better social responsibility, education, improved systems to prevent such infection and uniform availability of diagnostic resources for early diagnosis and management before complications sets in.

References

1. Chris pal A, Boor uGu H, Gopinath KG, Chandy S, Prakash JA, Thomas EM, Abraham AM, Abraham OC, Thomas K. Acute un differentiated febrile illness in adult hospitalized patients: the disease spectrum and diagnostic predictors - an experience from a tertiary care hospital in South India. Trop Dr. 2010;40(4):230–4.

2. Leelarasamee A, Chupaprawan C, Chenchittikul M, Udompanthurat S. Etiologies of acute undifferentiated febrile illness in Thailand. Journal of the Medical Association of Thailand = Chotmaihet Thangphaet. 2004; 87 (5): 464–72.

3. Acestor N, Cooksey R, Newton PN, Menard D, Guerin PJ, Nakagawa J, Christophel E, Gonzalez IJ, Bell D. Mapping the aetiology of non-malarial febrile illness in Southeast Asia through a systematic review--terra incognita impairing treatment policies. PLoS One. 2012;7(9): e44269.

4. Liu L, Johnson HL, Cousens S, Perin J, Scott S, Lawn JE, Rudan I, Campbell H, Cibulskis R, Li M, et al. Global, regional, and national causes of child mortality: an updated systematic analysis for 2010 with time trends since 2000. Lancet (London, England). 2012;379 (9832): 2151–61.

5. Bell M, Archibald LK, Nwanyanwu O, Dobbie H, Tokars J, Kazembe PN, Reller LB, Jarvis WR. Seasonal variation in the etiology of bloodstream infections in a febrile inpatient population in a developing country. International journal of infectious diseases: IJID: official publication of the International Society for Infectious Diseases. 2001;5(2):63–9.

6. Bharti AR, Nally JE, Ricaldi JN, Matthias MA, Diaz MM, Lovett MA, Levett PN, Gilman RH, Willig MR, Gotuzzo E, et al. Leptospirosis: a zoonotic disease of global importance. Lancet Infect Dis. 2003;3 (12): 757–71.

7. Pradutkanchana J, Pradutkanchana S, Kemapan manus M, Wuthipum N, Silpapojakul K. The etiology of acute pyrexia of unknown origin in children after a flood. The Southeast Asian journal of tropical medicine and public health. 2003;34(1):175–8.

8. Bruce MG, Sanders EJ, Leake JA, Zaidel O, Bragg SL, Aye T, Shutt KA, Deseda CC, Rigau-Perez JG, Tappero JW, et al. Leptospirosis among patients pre

©2023, IJMACR

senting with dengue-like illness in Puerto Rico. Acta Trop. 2005;96(1):36–46.

9. Levett PN, Branch SL, Edwards CN. Detection of dengue infection in patients investigated for leptospirosis in Barbados. The American journal of tropical medicine and hygiene. 2000;62(1):112–4.

10. Dhingra B, Mishra D. Early diagnosis of febrile illness: the need of the hour. Indian Pediatr. 2011; 48 (11):845–9.

11. Cape ding MR, Chua MN, Hadinegoro SR, Hussain II, Nallusamy R, Pitisuttithum P, Rusmil K, Thisyakorn U, Thomas SJ, Huu Tran N, et al. Dengue and other common causes of acute febrile illness in Asia: an active surveillance study in children. PLoS Negl Trop Dis. 2013;7(7):e2331.

12. Suttinont C, Losuwanaluk K, Niwatayakul K, Hoontrakul S, Intaranongpai W, Silpasakorn S, Suwan charoen D, Panlar P, Saisongkorh W, Rolain JM, et al. Causes of acute, undifferentiated, febrile illness in rural Thailand: results of a prospective observational study. Ann Trop Med Parasitol. 2006;100(4):363–70.

13. Zaidi AK, Awasthi S, deSilva HJ. Burden of in fectious diseases in South Asia. BMJ (Clinical research ed). 2004;328(7443):811–5.

14. Perkins GD, McAuley DF, Davies S, Gao F. Discrepancies between clinical and postmortem diag noses in critically ill patients: an observational study. Crit Care 2003; 7:129 –32.

15. Dimopoulos G, Piagnerelli M, Berre´ J, Salmon I, Vincent JL. Post mortem examination in the intensive care unit: still useful? Intensive Care Med 2004; 30:2080 –5.

16. Wangdi K, Kasturiaratchi K, Nery SV, Lau CL, Gray DJ, Clements AC. Diversity of infectious a etio logies of acute undifferentiated febrile illnesses in south and Southeast Asia: a systematic review. BMC in fectious diseases. 2019 Dec;19(1):1-7.

17. George R. Clinical spectrum of dengue infection. Dengue and dengue hemorrhagic fever. 1997:89-113.

18. Shedge R, Kavishwar V, Dhume V, Patil L. Pathology of Dengue Fever- Autopsy Study in a Tertiary Care Hospital. Global Journal For Research Analysis. 2017 January;6(1) : 45-47.

19. Torgersen C, Moser P, Luckner G, Mayr V, Joc Berger S, Hasib Eder WR, Dünser MW. Macroscopic postmortem findings in 235 surgical intensive care patients with sepsis. Anesthesia & Analgesia. 2009 Jun 1; 10 8(6):1841-7.

20. Saha A, Amonkar GP, Desai H, Baro B, Agrawal R. Acute respiratory distress syndrome: A study of autopsy findings. Lung India 2021; 38:442-7.

21. Sachdev S, Pandit SP. Acute respiratory distress syndrome: An autopsy study. J Postgrad Med Educ Res 2014; 48:8 13.

22. Estenssoro E, Dubin A, Laffaire E, Canales H, Sáenz G, Moseinco M, et al. Incidence, clinical course, and outcome in 217 patients with acute respiratory distress syndrome. Crit Care Med 2002; 30:2450 6.

23. Singh G, Gladdy G, Chandy TT, Sen N. Incidence and outcome of acute lung injury and acute respiratory distress syndrome in the surgical intensive care unit. Indian J Crit Care Med 2014; 18:659 65.

24. Flint A, Colby TV. Surgical pathology of diffuse infiltrative lung disease. Grune & Stratton, Incorporated; 1987.

25. Janigan DT. Giant cell pneumonia and measles: an analytical review. Canadian Medical Association Journal. 1961 Sep 9;85(13):741.

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Abbreviations

1. AFI- Acute Febrile Illness
2. AUFI-Acute undifferentiated febrile illness
3. ARDS- acute respiratory distress syndrome
4. ATN- acute tubular necrosis
5. DIC- Disseminated intravascular coagulation
6. HPF- High power field
7. MRSA- methicillin resistant staphylococcus aureus
8. RBC- Red blood cells

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