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Original Research Article

Evaluation of prolonged febrile illness in elderly

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ABSTRACT

Background: Febrile illness in elderly patients in hospitals is a challenge to the physician for diagnosis and treatment due to high morbidity as well as mortality and it increases if the febrile illness is prolonged. So proper evaluation and effective management is necessary for a better outcome. Keeping in mind the scarcity of studies in elderly febrile illness in India this study was taken up.
Method: A prospective study was designed in medical ICU of S.C.B Medical college and Hospital, Cuttack Odisha, India. 50 patients were included in this study from July 2007 to December 2008. Institutional Ethics Committee cleared the study.
Results: In 50 elderly (Age>60 yrs) patients of prolonged febrile illness, 36 (72%) were male and 14 (28%) were female. All had fever for >21 days. Pallor was the commonest sign (62%). 30 patients had infectious etiology, 15 had malignancies. Tuberculosis was the commonest infection (28%) comprising of 46.66% of infectious etiology with Pulmonary Tuberculosis (PTB) in 20% and Extrapulmonary Tuberculosis (ETB) in 26.66%. Malignancies accounted for 30% of cases with Non-Hodgkin's lymphoma (NHL) in 33.33% being the commonest amongst the malignancies. On follow up of 50 patients 21 (42%) got cured.
Conclusion: Febrile illness in elderly needs carefully evaluation as infections account for most of the cases and Tuberculosis in our part of India as a major cause in these patients is treatable. Malignancies remain the second most common cause where timely intervention goes a long way in reducing morbidity and mortality.

Keywords: Elderly, Malignancy, Non-infectious, Prolonged febrile illness, Tuberculosis

INTRODUCTION

Getting old is a natural and inevitable process as infancy or childhood where progressive impairment of functions results in loss of adaptive responses to stressors. As to who is elderly the cut-off point has been put at 60 yrs by United Nations for global comparison between countries.[1] Also WHO defines elderly people as who are more than 60 years of age.[2] In almost all gerontological literatures people above 60 yrs. of age are called elderly and senior citizens. Between 2000 to 2030 the number of older population is expected to increase from 420 million to 974 million. In Indian Census, in 2001 elderly population was 76.62 million and the number is expected to increase from 76 million in 2001 to 171 million by 2026.[3] A majority of the elderly people i.e. 88% live in rural areas. In India, the elderly population suffers from communicable as well as noncommunicable diseases. A decline in immunity as well as age related changes with other factors like social, cultural, economic, lake of adequate health care for these people put a heavy burden as the health care fabric of the country. As the elderly

population is expected to rise in future all over the world and more so in India due to increase in longevity by better health care focus will be on geriatric diseases and in tropical countries like ours specially in febrile illness.

METHODS

- After inclusion of patient's with informed consent, oral temperature will be recorded 6 hours.
- A diagnostic work up including detailed history, clinical examination, routine laboratory tests, urine analysis, relevant cultures, serology, chest radiography and abdominal ultrasound will be done.
- In non-revealing cases based on potential diagnostic clues special diagnostic tests will be taken up. Only diagnoses that are evidence based or clinically nearest will be retained.

Inclusion criteria

- Elderly patients (Age ≥60 years) presenting with febrile illness of more than 3 weeks will be taken up for the study.
- Patients should have documented temperature exceeding 101ºF (38.3ºC) on more than 3 occasions.
- No diagnosis at presentation.

Exclusion criteria

- Correct etiologic diagnosis already established by referring physician or institute.
- Nosocomial fever.
- Known / diagnosed HIV Infection.

Investigations

Routine

- Hb%, DC, TLC, Peripheral Smear Examination
- ESR
- FBS 2 hr. PPGBS & HBA1c
- Urine analysis
- Liver function tests
- Serum Urea & Creatinine
- PPD Skin test
- HIV Elisa
- Cultures- Blood/ Urine/ Sputum/ Fluids as appropriate
- Chest X-ray
- USG of Abdomen & Pelvis.

Special: Investigations to be done or required

- Transthoracic and Transesophageal Echocardiography
- CT Scan of Abdomen / Chest / Pelvis
- FNAC / Biopsy of suspected lympnode / mass
- Bone marrow examination
- Serum protein electrophoresis
- Serological tests (ANA, RA factor, Serum ACE Level etc.)
- Upper G.I. Endoscopy / Colonoscopy.
- Any other specialised lab/Imaging procedure as applicable based on clinical clues (e.g. CSF study)

RESULTS

The present study was conducted in the Postgraduate Department of medicine, SCB Medical College, Cuttack. During the period of study 52 elderly patients (age >60 years) admitted to medicine ward with prolonged fever were evaluated in the study. Two patients were excluded because of HIV positivity. All data were analysed with SPSS 16 windows software version.

Table 1: Mean age at presentation (in years).

Gender (Age in Yrs)	
Male (n=36)	65.97±4.218
Female (n=14)	64.50±3.082
Total (n=50)	65.55±3.953

Table 2: Age group distribution.

Age in Years	Male		Female		Total	
	No	%	No	%	No	%
60 - 64	10	20	4	8	14	28
65 - 69	19	38	10	20	29	58
70 - 74	2	4	0	0	2	4
75 - 79	4	8	0	0	4	8
>80	1	2	0	0	1	2

Mean age at presentation was 65.55±3.953 years for males mean age was 65.97±4.218 for females and mean age was 64.50±3.082years as represented in Table 1 and the distribution according to age group is represented in Table 2 with maximum number of patients in 65 to 69 years age group in our study.

Commonest symptoms in the study are weakness (8%), weight loss (8%), cough with expectoration (8%), headache and drowsiness (8%), followed by non-productive cough (6%), joint pain (6%), chest pain (6%) and dyspnoea (6%) as represented in Figure 1.

Commonest clinical sign in our study other than fever in the study was pallor (62%) followed by respiratory findings (22%), splenomegaly (18%), hepatomegaly (14%), lymphadenopathy (14%), neck rigidity (8%), arthritis (8%), gallop rhythm (6%) and icterus (4%) as represented in Figure 2.

Investigations in our study revealed Mean Haemoglobin value of 9.208±2.3979 gm/dl, with males having 9.089±2.6612 gm/dl and having females 9.514±1.5703 gm/dl, as represented in Table 3. Minimum TLC count in the study was 800/cumm and maximum value was

90700/cumm. With a Median value of 8750/cumm as represented in Table 4. Mean ESR in the study was 85.20±42.275 mm / 1st hr with males it was 85.03±46.557 mm/1st hr and for females it was 85.64±50.872 mm/1st hr as represented in Table 5.

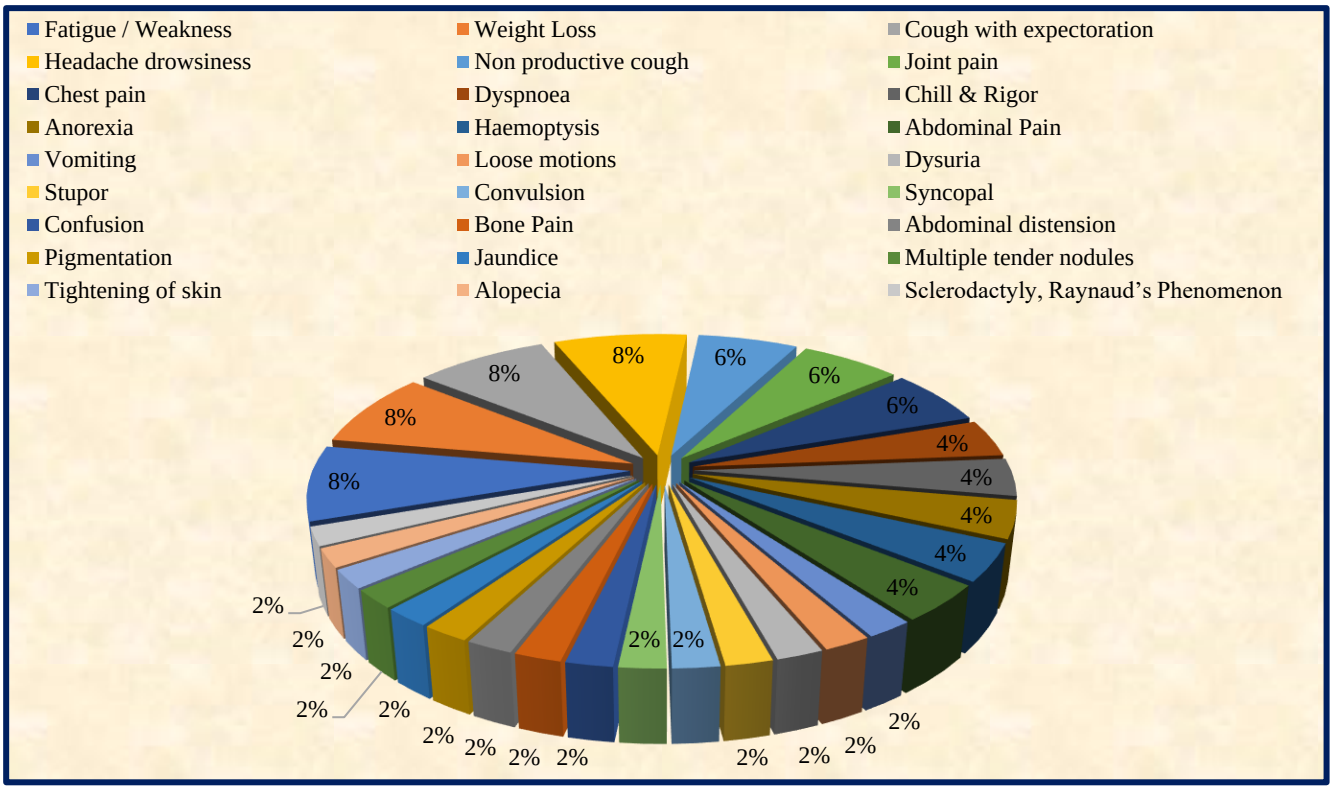

Figure 1: Symptoms other than fever in the study.

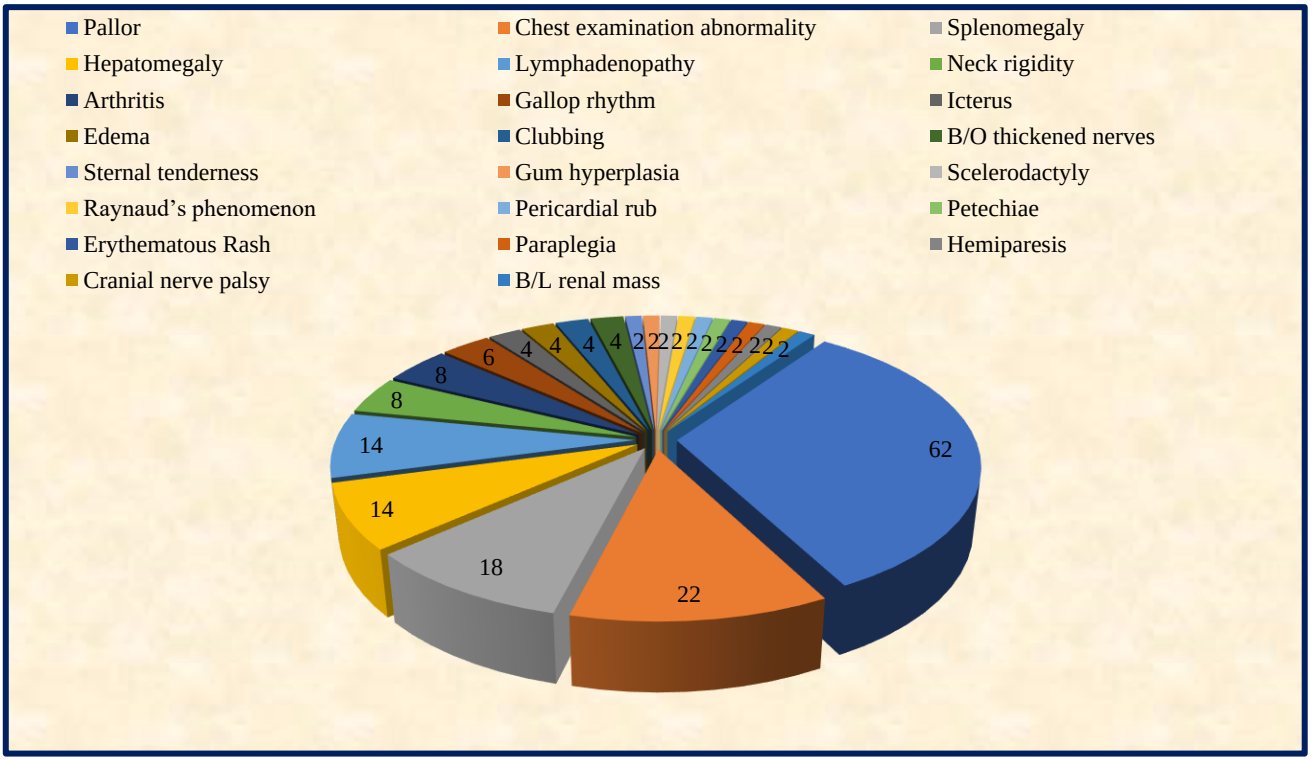

Figure 2: Clinical signs in elderly febrile patients.

In this study among the 50 elderly patients 30 (60%) were diagnosed to have infectious etiology in male 21 (42%) patients and female 9 (18%) patients. 15 patients were diagnosed to have malignancies and in male 12 (24%) female 3 (6%) patients. Non-infectious inflammatory disease comprised 2 cases (4%) and all were females. Miscellaneous cause was found in 2 cases (4%) all being males. Diagnosis could not be made in one case (2%) as represented in Table 6.

Table 3: Mean Haemoglobin (Hb).

Gender	Haemoglobin (in gm/dl)
Male (n=36)	9.089±2.6612
Female (n=14)	9.514±1.5703
Total (n=50)	9.208±2.3979

Table 4: Mean Total Leukocyte Count (TLC).

Gender	Mean total leukocyte count (In Thousands cumm)
Male (n=36)	11800±14600
Female (n=14)	9107.14±3263
Total (n=50)	11020.48±12517

Table 5: Mean Erythrocyte Sedimentation Rate [ESR] (in mm / 1st hr).

Gender	ESR (in mm/1st hr)
Male (n = 36)	85.03±46.557
Female (n = 14)	85.64±50.872
Total (n = 50)	85.20±42.275

Table 6: Diagnostic groups.

	Male		Female		Total	
	No	%	No	%	No	%
Infections	21	42	9	18	30	60
Malignancies	12	24	3	6	15	30
Non-infectious inflammatory disease	0	0	2	4	2	4
Miscellaneous	2	4	0	0	2	4
No diagnosis	1	2	0	0	1	2

In the present study tuberculosis (46.66%) was the commonest of the infections with ETB in 26.66%, while PTB was found in 20% of cases among infections. Next common etiologies were abdominal abscesses (10%), enteric fever (10%), infective endocarditis (6.66%) and ENL (6.66%). Other minor etiologies were urinary tract infection, respiratory infection, vivax malaria, falciparum malaria comprising one case each respectively (3.33%) as represented in Table 7.

In the present study malignancies accounted for 30% of cases (n=15). Among the malignancies most common was NHL 33.33% of cases (n=5), next common was MM 20% of cases (n=3). Other malignancies were AML (13.33%), CLL (6.6%) and lung cancer, brain & spinal metastasis, atrial myxoma, gastric lymphoma and carcinoma of stomach having incidence of 6.6% each. In the study haematological malignancies accounted for 73.33% of cases (n=11) as represented in Table 8.

Table 7: Infection categories (n = 30).

	Male		Female		Total	
	No	%	No	%	No	%
PTB	4	13.33	2	6.66	6	20
ETB	6	20	2	6.66	8	26.66
Infective Endocarditis	2	6.66	0	0	2	6.66
Erythema Nodosum Leprosum (ENL)	2	6.66	0	0	2	6.66
Enteric Fever	2	6.66	1	3.33	3	10
UTI	1	3.33	0	0	1	3.33
Respiratory Infection	1	3.33	0	0	1	3.33
Vivax Malaria	0	0	1	3.33	1	3.33
Falciparum malaria	1	3.33	0	0	1	3.33
Liver abscesses	1	6.66	0	0	2	6.66
Splenic abscesses	1	3.33	0	0	1	3.33
Infection of unknown focus	2	6.66	0	0	2	6.66

Table 8: Malignancy (n = 15).

	Male		Female		Total	
	No	%	No	%	No	%
NHL	5	33.33	0	0	5	33.33
Multiple Myeloma (MM)	2	13.33	1	6.66	3	20
Acute Myeloid Leukemia (AML)	2	13.33	0	0	2	13.33
Chronic Lymphocytic Leukemia (CLL)	1	6.66	0	0	1	6.66
Lung Cancer	1	6.66	0	0	1	6.66
Atrial Myxoma	0	0	1	6.66	1	6.66
Gastric Lymphoma	0	0	1	6.66	1	6.66
Ca stomach	1	6.66	0	0	1	6.66
Brain and Spinal metastasis	0	0	1	6.66	1	6.66

On follow up 21 patients (42%) were cured (all of them having infectious etiology), 8 patients (16%) were lost to

follow up, 7 patients (14%) are still on treatment, 4 patients (8%) died (Malignancy - 2, Infection- 1, No diagnosis- 1), 3 patients (6%) are on follow up, 3 patients (6%) were referred to other departments for treatment, 2 patients (4%) were put on chemotherapy for malignancy but subsequently lost to follow up and one patient (2%) was operated for gastric malignancy as represented in Table 9.

Table 9: Follow up (for upto 6 months).

	No.	%
Cured	21	42
Lost to follow up	8	16
On treatment	7	14
Died	4	8
On follow up	3	6
Referred	3	6
On Chemotherapy, subsequently lost to follow up	2	4
On Chemotherapy	1	2
Operated	1	2
Total	50	100

DISCUSSION

The present study Evaluation of prolonged febrile illness in the elderly has been undertaken in the Postgraduate Department of Medicine, SCB Medical College, Cuttack from July 2007 to December 2008. During this period after exclusion of few patients, 50 elderly patients (age >60 years) admitted to Medicine ward with prolonged fever (fever >21 days) were taken up for study.

All patients were evaluated with detailed history, clinical examination and relevant investigations as outlined and patients were followed up for 6 months.

In the present study mean age of the study group was 65.55±3.95 years. (M: 65.97±4.21, F: 64.50±3.08). In the Chen Y et al, mean age was 70 years.[4]

In the present study age group 60-64 years comprised of 14 patients (28%), [M: 10 (20%) and F:4 (8%)]. 29 patients were in the age group 65-69 years [M: 19 (38%) andF:10 (20%)]. In the age group 70-74 years there were 2 patients (4%), [all male] and 4 patients (8%) were in the age group 75-79 years [all male]. Only one patient was above the age of 80 years. Common presenting symptoms in elderly prolonged febrile illness (>21 days duration) in our study were fatigue/ weakness (8%), weight loss (8%), cough with expectoration (8%), headache and drowsiness (8%), non-productive cough (6%), joint pain (6%), chest pain (6%), dyspnoea (4%), anorexia (4%), haemoptysis (4%) and chill with rigor (4%).

In the present study pallor was the commonest clinical sign (other than fever) present in 31 (62%) of elderly patients followed by respiratory system findings 11 (22%), splenomegaly in 9 (18%), hepatomegaly 7 (14%), lymphadenopathy in 7 (14%), neck rigidity in 4 (8%) and arthritis in 4 (8%). Less common findings were gallop rhythm (6%), sternal tenderness (2%), gum hyperplasia (2%), sclerodactyly (2%), Raynauds phenomenon (2%), pericardial rub (2%), petechiae (2%), erythmatous rash (2%), paraplegia (2%), hemiparesis (2%) and multiple cranial nerve palsy (2%).

In the current study mean Hb. was 9.208±2.399 gm/dl, for males 9.089±2.6612 gm/dl and for females 9.514±1.5703 gm/dl & in the study mean TLC count was 11020.48±12517 per cumm. For males it was 11800±14600 per cumm, and for females 9107.14±3263.661 per cumm. Minimum value was 800 per cumm, maximum value was 90700 per cumm with Median of 8750 per cumm.

The present study revealed mean ESR of 85.20±42.275 mm/hr [M: 85.03±46.557 mm/hr & F:85.64±50.872 mm/hr]. In the study by VanderschuerenS et al (n=290) mean ESR was 79 (range 46-108).[5]

In this study among the 50 elderly patients 30 (60%) were diagnosed to have infectious etiology [M: 21 (42%) ,F: 9 (18%)]. 15 patients were having malignancies- [M:12 (24%), F: 3 (6%)]. Non-infectious inflammatory diseases comprised 2 cases (4%) [all females]. Miscellaneous causes were found in 2 cases (4%) [all males]. Diagnosis could not be made in one case (2%).

In the present study infection was the cause in 60% of cases, which is significantly higher than other studies like that of 50.6% in Chen et al, 40.29% in Saxena et al, 36% in Esposito and Gleckman et al, 35% in Knockaert et al, 45.5% in OnallK et al, study.[4,6-9] In all the studies infection was the main cause for prolonged febrile illness in elderly.

Malignancies were the second highest diagnostic category i.e. 30% of patients in our study which is concordant with studies by Chen et al 10.3%, Saxena et al 29.85%, Esposito & Gleckman et al 24%, Knockaert et al 19%, OnallK et al, 4.5%, 10.3%.[4, 6-9]

Non-Infectious Inflammatory Diseases(NIID) in the present study comprised of 4% of the cases which was similar to the study by chen et al.[4] The study by Saxena et al 4.49% revealed higher value in comparison to our study.[6] Our study was comparable to studies by Esposito and Gleckman et al, 26% and Knockaert et al, 28% and onallk et al. [7-9]

Miscellaneous causes group in the present study comprised 4% of elderly patients (n=50) which was comparable to the study of Chen et al, 5.7%, Saxena et al 14%, Esposito & Gleckman et al 9%, Knockaert et al 8%.[4,6-8] No diagnosis could be made in 2% of elderly patients in the present study. This group was significantly lower compared to other studies by Chen et al, 28.7%,

Saxena et al, 13.48%, Esposito and Gleckman et al, 5% and Knockaert et al, 9%.[4,6-8]

In the current study tuberculosis was the commonest infection found in 14 patients (28%), comprising 46.66% of infections. Out of 14 tuberculosis patients, PTB (35.71%) was commonest, followed by tubercular meningitis (28.57%) and tuberculosis of undermined site (14.23%). While miliary tuberculosis, pericardial effusion and adrenal tuberculosis were found in one case each (7.14%).

Chen et al, 29.54% and Esposito and Gleckman et al, 20% cases of infections were due to tuberculosis among elderly patients with prolonged fever.[4,7] while OnallK et al reported 60% of infectious etiology were due to tuberculosis.[9]

In the study among adult patients with prolonged fever from North India, Handa R et al, reported tuberculosis as cause in 49% of cases.[10] Our study was also comparable to the study by Arora VK et al, and Khilnani GC et al, which is comparable to our study.[11,12]

Esposito and Gleckman et al, reported 31.7% in his study.[7] Knockaert et al, also reported abdominal abscess were the commonest infectious cause for prolonged fever in elderly i.e. 34.72% of infectious group (n=72).[8] In the present study abscesses were found in 10% cases (n=3) of infection etiology. Two of them were due to liver abscess and one was due to splenic abscess. Our study was comparable to the study by Baron M J et al.[13]

Infective Endocarditis was found in 14 cases i.e. 19.44% of infections etiology (n=72) in the study by Knockaert et al, whereas in the present study it was 6.66% which is lower.[8] The study by Karchmer AW et al, showed similar results with our study.[14]

Other causes among infectious etiology in current study are enteric fever (10%) ENL (6.6%), Malaria (6.66%), urinary tract infection (3.33%), respiratory infection (3.33%) while no focus could be found in 6.66%.

In the present study malignancies accounted for 30% cases (n=15). Among the malignancies most common was NHL 33.33% of cases (n=5), next common was MM 20% of cases (n=3). Other malignancies were AML (13.33%), CLL(6.6%), lung cancer, brain and spinal metastasis (6.6%), atrial myxoma (6.6%), gastric lymphoma (6.6%) and Ca - stomach (6.6%). In this study, haematological malignancies accounted 73.33% of cases (n= 11).

Chen et al, reported intestinal cancer (33.33%) as the commonest cause of geriatric prolonged fever with malignancy followed by lung cancer, thyroid cancer with metastasis and malignant abdominal tumour with extensive metastasis.[4]

In the study by Esposito and Gleckman et al, lymphoma was the most common cause of geriatric prolonged fever (58% of cases of Neoplasms) followed by renal cell carcinoma, atrial myxoma, hepatoma and carcinoma of the intestinal tract.[7] In their series of 26 cases of neaplasms causing prolonged fever in elderly, Esposito and Gleckman et al, also noted that NHL (31%) was slightly more common than Hodgkin's lymphoma (27%).[7]

Knockaert et al, reported 37 cases (19%) of neoplasms causing prolonged fever in the elderly in which hematological malignancies were responsible for 19 cases and solid tumours were responsible for 18 cases.[8] Wetzler M et al, study results was also comparable to our study.[15]

NIID /collagen vascular disease /connective tissue diseases were found in 2 cases (4%) in the present study. One was due to rheumatoid arthritis; other was Mixed Connective Tissue Disorder(MCTD). Both the cases were female.

Much lower incidence of NIID is reported from China and India. Chen et al, study group reported 4.6% of cases of NIID. Our study reported only 2 cases of NIID (4%).[4] Saxena et al, reported 1.49% cases in a study conducted in North India.[6]

Much higher incidence of (NIID) were reported from Europe, North America and Japan among the elderly patients with prolonged fever. Esposito and Gleckmanet al, 20% and Knockaert et al, 28% reported the incidence NIID in their studies.[7,8] Temporal arteritis was the commonest cause (64%) in Esposito and Gleckman et al.[7]

Miscellaneous cause was revealed in 2 cases (4%) in the present study. One was hypoplastic anaemia and the other was myelodysplastic syndrome (Refractory cytopenia with multilineage dysplasia).

On the follow up for 6 months, 21 patients (42%) got cured(all of them having infectious etiology), 8 patients (16%) were lost to follow up, 7 patients (14%) are still on treatment, 4 patients (8%) died (Malignancy - 2, Infection -1, No diagnosis- 1), 3 patients (6%) are on follow up, 3 patients (6%) were referred to other departments for treatment, 2 patients (4%) were put on chemotherapy for malignancy but subsequently lost to follow up and one patient (2%) was operated for gastric malignancy and is on chemotherapy.

CONCLUSION

The prolonged febrile illness in the elderly is a major diagnostic challenge and dilemma to the physician. Current studies show that most of the cases of prolonged fever in the elderly can be diagnosed with meticulous history taking, detailed clinical examinations and investigations based on the potential diagnostic clues. Infection is the predominant cause followed by

malignancy. The incidence of tuberculosis is much more common in the elderly than their younger counter- parts in India. Prolonged pyrexia due to connective tissue disorders in the elderly in the present study is much less common when compared to the data in western literature. The percentage of cases for which a cause is never identified in the elderly patients is significantly lower than it is in the younger patients.

The elderly people have increased susceptibility to many diseases usually not encountered in the younger age group and are at significantly increased risk for morbidity and mortality due to delays in diagnosis and management. Early recognition and prompt clue related investigations of the prolonged febrile illness in the elderly are the cornerstones to make an early diagnosis whenever possible, thus reducing sufferings in the elderly, who are already compromised with low physiological reserves due to the process of ageing and frequent presence of co morbid illnesses. Studies involving larger number of patients in future will throw more light in this aspect of health in the elderly.

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