

Analysis of Geriatric Infections and a Guide to Empirical Antibiotic Therapy

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ABSTRACT

BACKGROUND

Elderly people have increased susceptibility to infection and are at significantly increased risk of morbidity and mortality due to various common infections. Urinary tract and respiratory tract infections predominate in elderly people. Gram negative pathogens especially *E. coli* are commonly observed pathogens. In gram positive infections, staphylococcus is usually isolated from skin and soft tissue infections.

METHODS

Data was collected prospectively between the months of March 2015 and August 2016. Patient demographics and clinical data were recorded from oral questionnaires and hospital records. 219 patients satisfied the inclusion criteria. All patients were subjected to basic investigations with blood and urine cultures at the time of admission. Other cultures like respiratory or pus cultures were collected as and when needed. Specific investigations such as ultrasound abdomen, computed tomography kidneys, ureters and bladder (CT KUB), CT thorax, echocardiography, neuroimaging and procalcitonin were done in certain patients when required.

RESULTS

Of the 219 patients included in this study, 127 (58 %) were males and 92 (42 %) were females. Mean age of the study population was 72.40. The most common source of bacteraemia was urinary in 33 % and was unknown in 25 %. The most common organism isolated in blood culture was *Staphylococcus aureus* followed by *E. coli*. Respiratory infections had unidentified pathogens in 81 % of patients. The most common organism isolated from respiratory secretions was klebsiella followed by acinetobacter and pseudomonas. 11 % of patients developed multi organ dysfunction syndrome of which urinary and respiratory systems were the most common primary sources of infection.

CONCLUSIONS

A significant incidence of unidentified source of infection was observed. Staphylococcus bacteraemia was a significant observation as *E. coli* is reported to be common. Urinary tract and respiratory infections were seen to be associated with increased incidence of multiorgan dysfunction.

KEYWORDS

Elderly, Febrile Illness, *Staphylococcus aureus*, *Escherichia coli*, Multiorgan Dysfunction

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BACKGROUND

Compared to younger population, elderly people have increased susceptibility to infection and are at significantly increased risk for morbidity and mortality due to various common infections. Low physiological reserves due to the biologic changes that accompany aging and the frequent presence of comorbid illnesses contribute to the outcome.¹ Morbidity and mortality rates also are influenced by age and comorbidity-related decremental changes in host defences. Older adults are at greater risk for hospitalisation, which can in turn be complicated by nosocomial infections. Elderly people are also at increased risk for adverse drug reactions; in clinical geriatrics, even with careful consideration, patients may be treated with multiple medications.² In addition, there are biological changes that occur with age which alter the pharmacology of many classes of drugs, including antibiotics.

A delay in diagnosis and initiation of appropriate treatment due to atypical presentation may lead to increased morbidity and mortality.³ Prevention, early recognition and prompt initiation of empirical antimicrobial therapy are the cornerstones of the strategy to reduce the impact of infectious diseases in elderly.⁴ However, early recognition and avoidance of diagnostic delays may be problematic in this age group, since atypical presentations of acute diseases are common. Virtually any acute change in functional status may indicate the onset of a serious infectious disease.⁵ For example, changes in cognitive function from baseline are commonly seen, even when the infection does not involve the central nervous system. Furthermore, pneumonia may present without cough or increased sputum production, and lower-tract urinary infection may occur without urgency, frequency or dysuria. A common factor for all acute infections in the elderly is that up to one-third of patients may present without a clear febrile response. Fluctuations in body temperature and afebrile episodes prior to other symptoms complicate the outcome. The present study was done to analyse the various clinical presentations, organisms isolated and outcome of febrile illness in elderly.

METHODS

This study was a prospective observational study done in the Department of General Medicine, Sri Ramachandra Medical College and Research Institute with patients admitted between March 2015 and August 2016. Clearance was obtained from institutional ethics committee. All patients above the age of 65 years, with a history of fever and / or a documented oral temperature of 99 degrees F or more within the first 48 hours of hospitalisation were included in the study. Data was collected prospectively between the months of March 2015 and August 2016. Patient demographics and clinical data were recorded from oral questionnaires and hospital records, recorded into a case sheet. A proforma containing detailed information of each patient was designed according to the study protocol. 219 patients satisfied the inclusion criteria and were included in

the study. All patients were subjected to basic investigations which included complete blood count (CBC), renal function test (RFT), liver function test (LFT), coagulation profile (PT, PTT, INR), serum electrolytes, urine routine, blood and urine cultures at the time of admission. Other cultures like respiratory or pus cultures were collected as and when needed. Specific investigations such as ultrasound abdomen, CT KUB, CT thorax, echocardiography, neuroimaging, procalcitonin and other serological tests were done in certain patients as and when required. Data was entered into Microsoft Excel data sheet and was analysed using Statistical Package for the Social Sciences (SPSS) 22 version software. Categorical data was represented in the form of frequencies and proportions. Continuous data was represented as mean.

RESULTS

Of the 219 patients included in this study, 127 (58 %) were males and 92 (42 %) were females. 151 patients (71 %) were between the ages of 65 to 75 years and only 8 patients (4 %) were above the age of 85 years. Mean age of the study population was 72.40. 131 patients (61 %) presented with 3 to 7 days of fever. Fever for more than 14 days was seen in 12 (5 %) of the patients. 89 % of the patients had comorbid illnesses of which diabetes mellitus (DM) and systemic hypertension (HTN) were the most prevalent. Consciousness as assessed by Glasgow Coma Scale was intact in 171 (78 %) of patients and impaired in 48 (22 %) of patients. Of the 127 diabetic patients admitted with fever, 31 % were found to have very poor glycaemic control with glycated haemoglobin test (HbA1c) greater than 9.

Anaemia (less than 10 g / dL) was seen in 50 (23 %) of patients. Thrombocytopenia (less than 1,00,000 cells per cubic mm) was seen in 35 (16 %) of patients. 4 % of patients presented with hypoglycaemia and 24 % with blood sugars greater than 200. 89 patients (41 %) had serum creatinine more than 1.3 mg / dL. 81 patients had electrolyte abnormalities; metabolic acidosis was the most frequent (58 %) followed by hyperkalaemia (26 %). Deranged LFT was seen in 23 % of the patients of which elevated transaminase was the most common abnormality (54 %).

Tuberculous (TB) infection was seen in 7 patients (3 %) with pulmonary involvement being common. 73 patients (33 %) required to be admitted to the intensive care unit (ICU) based on the initial assessment. Of the patients admitted to ICU, 43 patients required inotropic support, 36 patients needed mechanical ventilation, 10 patients underwent at least 1 cycle of haemodialysis (HD) and 2 patients required extra corporeal membrane oxygenation (ECMO). Respiratory infections were the most prevalent accounting for 32 % of the patients in this study followed by urinary infections in 27 % of the patients. 87 (40 %) patients had an identifiable organism in either blood, urine, sputum or pus culture. 24 (11 %) patients showed growth of an organism in blood culture. *Staphylococcus aureus* was most frequently seen in 6 (25 %) of patients while *E. coli* was the most common gram-negative bacilli seen in 4 (17 %) of the 24 patients with bacteraemia. 67 (80 %) of the 84 patients with unstable vitals on admission recovered while 17 (20 %) died.

Category	No. of Patients	Percentage
Respiratory	69	32 %
Urinary	59	27 %
Other infection	43	20 %
Soft tissue	18	8 %
Gastrointestinal	10	5 %
Non-infectious	10	5 %
TB	7	3 %
Neurological	3	< 1 %
Total	219	

Table 1. Infections

Organism	No. of Patients	Percentage
<i>S. aureus</i>	6	25 %
<i>E. coli</i>	4	17 %
Acinetobacter	2	8 %
<i>Enterococcus faecalis</i>	2	8 %
Klebsiella	2	8 %
<i>Morganella morganii</i>	2	8 %
<i>Salmonella typhi</i>	2	8 %
<i>Citrobacter koseri</i>	1	4 %
Proteus	1	4 %
Pseudomonas	1	4 %
Streptococcus	1	4 %
Total	24	

Table 2. Blood Culture

Organism	No. of Patients	Percentage
<i>E. coli</i>	17	46 %
<i>Enterococcus faecalis</i>	6	16 %
Klebsiella	6	16 %
Proteus	4	11 %
Pseudomonas	3	8 %
<i>Citrobacter koseri</i>	1	3 %
Total	37	

Table 3. Urine Culture

Vitals on Admission	Count	Outcome		Total
		Recovered	Death	
Stable		135	0	135
	% within vitals on admission	100.0 %	.0 %	100.0 %
Unstable	Count	67	17	84
	% within vitals on admission	79.8 %	20.2 %	100.0 %
Total	Count	202	17	219
	% within vitals on admission	92.2 %	7.8 %	100.0 %

Table 4. Correlation between ICU Admission and Hospitalisation Outcome

Antibiotic	No. of Patients	Percentage
Extended Spectrum Beta Lactam	39	66 %
Carbapenem + Fluoroquinolone	6	10 %
Carbapenem + Linezolid	4	7 %
Fluoroquinolone	3	5 %
Carbapenem	3	5 %
3rd Generation Cephalosporin	2	3 %
Polymyxin + Fluoroquinolone	2	3 %
Total	59	

Table 5. Antibiotic Therapy

Diagnosis	Mortality	
	Number of Patients	Percentage
LRTI	6	9 %
UTI	4	7 %
BSI	2	25 %
SSTI	3	17 %
CNS Infection	1	33 %
Other (H1N1 Influenza)	1	20 %

Table 6. Mortality

Gram negative infections were common and cefoperazone-sulbactam followed by piperacillin-sulbactam were the most used empiric therapies to treat. Majority (60 %) of the patients received 5 to 7 days of antibiotics. Respiratory infections were the leading cause of death followed by urinary tract infection (UTI). 6 patients admitted with a respiratory infection died.

DISCUSSION

This study included 219 patients admitted in the Department of General Medicine between March 2015 and August 2016.

Of the 219 patients included in this study 127 (58 %) were males and 92 (42 %) were females.

71 % of the patients were between the ages of 65 and 75 years with the mean age of 72.4 years, which was comparable to that observed by Kucukardali et al,⁶ in their study of 330 elderly patients with community acquired infections where the average age was 76 years. Arun et al.,⁷ conducted a similar study, analysing 100 patients and observed that 79 % of the population was between 65 and 74 years. This was comparable to our study in which 71 % of the population was between 65 and 74 years. 61 % of the patients presented with 3 to 7 days of fever. Fever for more than 14 days was seen in 5 % of the patients.

In our study diabetes mellitus and systemic hypertension were the most frequently associated comorbid illnesses. 59 % of the patients had diabetes mellitus and 58 % had hypertension which is comparable to the observations of Kucukardali et al., who noted systemic hypertension in 42 % of their study population. However, the percentage of diabetes prevalent in our patients was higher than the 29 % observed by Kucukardali et al.

Avkan-Oguz et al.,⁸ documented that hypertension was observed in 39.12 %, diabetes in 28 % and coronary artery disease in 13.1 %. These discrepancies reflect the increased incidence of diabetes mellitus in the Indian population.

22 % of patients had decreased Glasgow Coma Scale (GCS) on admission whereas 18 % of patients presented with hypotension which was consistent with the findings of Norman et al. who stated that elderly patients with sepsis present with confusion more often than hypotension. Roeltgen et al.,⁹ proved that non-central nervous system infections may mimic central nervous system infections in elderly individuals by presenting with decreased consciousness.

Of the total study population, 33 % required ICU admission of which 43 patients required ionotropic support, 36 patients required mechanical ventilation, 10 patients underwent at least one cycle of haemodialysis and 2 patients required extra-corporeal membrane oxygenation.

We also found during the course of the study that 11 % of the patients developed multi-organ dysfunction syndrome (MODS). 39 % of patients who had a respiratory infection or urinary infection during presentation, developed MODS, whereas only 9 % with soft tissue infection developed MODS.

The most common infection was respiratory as seen in 32 % of our study population which is comparable to the finding of respiratory infection in 41 % of patients observed by Kucukardali et al. and 57 % by Arun et al. 27 % of our study population had urinary tract infections which was similar to the 27 % observed by Kucukardali et al. and 19 % by Arun et al. Bloodstream infection contributed to 11 % of the overall study population that presented with fever similar to the result observed by Kucukardali et al. who also noted 10 % of the population presenting with bloodstream infections. 5 % had gastrointestinal infections, 8 % had skin and soft tissue infections and less than 1 % had central nervous system infection, which was comparable to 10 %, 5 % and 2 % respectively, as observed by Kucukardali et al.

Yoshikawa et al.¹⁰ found UTIs to be the most common cause of bacteraemia in the geriatric population and this corroborated with the findings in our study where 33 % of the patients with bacteraemia had a urinary focus of infection. 25 % of patients who had bacteraemia did not have any identifiable source. Kucukardali et al. also found that gram negative organisms were the most commonly isolated in their study population with influenza being the most frequent. In our study, we found that *E. coli* was the most common gram-negative organism found in blood and urine samples of our study population.

On individual detailed analysis of blood and urine cultures, *E. coli* was the most common type of pathogen isolated from urine (17 cases in urine and 5 cases in bloodstream), which is comparable to the 29 cases in urine cultures and 5 cases in bloodstream as seen in Kucukardali et al. *Staphylococcus aureus* was isolated in 6 cases in blood cultures, which is comparable to the 13 cases in bloodstream infections as seen in Kucukardali et al. *Pseudomonas* was isolated in three cases in urine cultures comparable to the seven cases seen in Kucukardali et al. Another interesting observation of our study was that *E. coli*, klebsiella, pseudomonas and proteus were commonly isolated from urine cultures of patients who presented with sepsis and Nys et al.¹¹ found a similar result in their study. The causative organism could be isolated in a culture of respiratory secretion only in 19 % of these patients. In 81 % of the patients diagnosed to have respiratory infection, the causative organism was unknown. This finding was comparable to that of Niederman et al.,¹² who found that in 60 % of the population that presented with community-acquired pneumonia (CAP), the causative organism was unknown. With regard to skin and soft tissue infections (SSTI), 66 % patients had an organism isolated in pus culture of which *Staphylococcus aureus* was the most prevalent organism accounting for 58 % of the organisms grown in a pus culture.

52 % of the patients had leukocytosis, which is comparable to the finding of Mouton et al.,¹³ that 60 % of the elderly patients with fever had leukocytosis. In our study, we analysed the correlation between leucocytosis and bacteraemia and found that leucocytosis was a fairly good predictor of bacteraemia having a sensitivity of 83.3 %, specificity of 45.6 %, positive predictive value of 15.8 % and negative predictive value of 95.7 % with a significant P-value of 0.005, thus proving to be a good predictor. Terpenning et al.,¹⁴ found that although as many as 32 % of elderly patients with bacteraemia failed to demonstrate leukocytosis. 84 % exhibited a left shift; as defined by an excessive number of neutrophilic bands.¹⁴

On analysis of leucocytosis and bacteriuria, we found a P-value of 0.06 and hence not establishing a significant correlation between the same. However, it had a fairly good negative predictive value of 88.2 % and can be used as a reasonable indicator of the absence of bacteriuria even though a direct correlation cannot be seen. On a similar analysis of correlation between pyuria and bacteriuria, we found that pyuria was an excellent predictor of bacteriuria with a specificity of 92.9 %, positive predictive value of 67.5 % and negative predictive value of 94.4 % with a P-value

less than 0.001. This result was comparable to the findings of Juthani-Mehta et al.,¹⁵ who found 100 % negative predictive value of pyuria in correlation with bacteriuria.

Mean duration of hospital stay was 7.37 days, which was comparable to 8.6 days observed in Kucukardali et al., and 9.6 in Avkan-Oguz et al. The average hospital stay for bacteremic patients was 11 days with recovery being at 75 % and mortality at 25 %. However, Arun et al. showed a significantly lower hospital stay in blood culture positive patients with an average being 4 days. With regard to UTI, the average hospital stay was 8 days with 93 % patients recovering and 7 % mortality was noted. This is comparable to the results of Arun et al., which found the average duration of stay to be 4.75 days. The average length of hospital stay for respiratory infections was 6 days and 91 % recovered with only 9 % mortality.

The study by Arun et al. showed the average duration of stay in patients who presented with respiratory sepsis was 5 days, which is comparable. However, their study showed a mortality of 74 % in respiratory infections. The likely cause for the disparity between the findings of the two studies is that Arun et al., considered only patients with respiratory sepsis and did not include uncomplicated lower respiratory tract infections in their analysis. Mean duration of hospital stay for SSTI was 8 days. 83 % recovered with treatment and 17 % died. Kucukardali et al. observed a mean duration of hospitalisation of 10 days and 12 % mortality rate in SSTIs. Gastrointestinal infections had a mean stay in hospital of 4 days and 100 % recovery rate. CNS infections had an average stay of 11 days, which was far higher than that of Arun et al. who observed that CNS infections had an average period of hospitalisation of 3 days. This is possibly due to the early mortality in CNS infections noted in their study.

Out of the total study population, 92 % recovered at the end of treatment. 33 % required ICU admission. Of this population, 77 % recovered and 23 % died. 60 % of the patients received a course of antibiotics lasting 5 - 7 days and this timely, effective and adequate treatment resulted in the reduced mortality seen in this study as compared to other studies across the world of similar nature and type. The overall mortality seen in our study was 8 %. Mortality observed by Kucukardali et al. was close to 17 %. When the overall stay in hospital was analysed, 97 % recovered if the duration of stay was less than 7 days and mortality was 3 %. When the stay in hospital was more than 7 days, 83 % of the population showed recovery, however, there was an increase in mortality to 17 %. Thus, there is a significant correlation between the duration of hospital stay and outcome (P-value 0.001). We infer that prolonged stay in hospital is associated with an increased risk for mortality. The correlation between ICU admission and mortality was extremely significant with P value less than 0.001.

CONCLUSIONS

The most common focus of infection in elderly people was respiratory (32 %) followed by urinary (27 %). Leucocytosis had a strong correlation with bacteraemia. The correlation between pyuria and bacteriuria was found to be strongly

significant with a specificity of 92.9 % and a negative predictive value of 94.4 %. *E. coli* was the most frequently isolated urinary pathogen accounting for 46 % of bacteriuria. *Enterococcus faecalis* was the next most common followed by other gram-negative bacilli such as klebsiella, proteus and pseudomonas. Mortality was higher in respiratory infection. Urinary tract and respiratory infections were seen to be associated with increased incidence of multiorgan dysfunction. The correlation between prolonged stay in hospital (more than 14 days) and mortality was statistically significant. The correlation between unstable vitals on admission and mortality was also highly significant. The relation between ICU admission and mortality was also highly significant.

The strengths of this study are a suitable sample size of 219 patients which was comparable to most other similar studies from all over the world. The limitation of the study is that it did not include elderly patients with infections who did not develop febrile response, which could have been possible only as a retrospective study.

Data sharing statement provided by the authors is available with the full text of this article at jebmh.com.

Financial or other competing interests: None.

Disclosure forms provided by the authors are available with the full text of this article at jebmh.com.

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