

Atypical Presentations of Acute Infections in Hospitalized Older Adults: The Prevalence, Predictors, and Outcomes

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Abstract

Background/ purpose: Atypical presentation of acute infections, is a well-known phenomenon in older people. It is extensively recognized in the literature but lacks sufficient attention in recent clinical research. Reaching a disease-specific diagnosis in those with subtle, nonspecific, or atypical presentations is a major challenge. The aim of this study was to report the prevalence of different presentations of acute infections among hospitalized elderly patients, and the factors associated with atypical presentation.

Methods: a retrospective medical records review of 220 patients diagnosed with acute infection. The presenting symptoms for each type of infection were reported. Data regarding medical comorbidities, cognition, frailty, and functional status were obtained. Factors associated with the atypical presentation were evaluated.

Results: Urinary tract infections and community-acquired pneumonia accounted for 44.5% and 25.5% infections, respectively. The patients presented with atypical symptoms in absence of classical symptoms represented 35.5% of the cases. 64.5% of the participants had an absent febrile response. Decreased oral intake was the most prevalent atypical complaint followed by unexplained new-onset functional decline. Dementia and frailty were independent predictors for atypical presentations.

Conclusions: Older adults present acute infections differently. Many common infections present as delirium, new functional decline, new or worsened incontinence [urine, fecal], anorexia, or falls, especially in patients with dementia and frailty. Fever is usually absent in the elderly with acute infections. Moreover, infections in the elderly may present as an exacerbation of chronic stable medical illness e.g. congestive heart failure or diabetes. The in-hospital mortality is higher among those having atypical presentations.

Keywords:

Infections in elderly, atypical presentation, pneumonia, Urinary tract infections

Background

Older adults are at increased risk of infection, which is a leading cause of morbidity and mortality in this age group.^[1] The increased infections related mortality in elderly is attributed to multiple factors, including: immunosenescence, medical comorbidities, undernutrition, functional decline, frailty, and increased adverse drug events^[2].

Reaching a final disease-specific diagnosis, remains a clinical dilemma when managing older adults. According to Fried et al., less than half of the elderly patients fitted into the classical medical model where the presenting symptoms and signs can refer immediately to a certain disease.^[3] In the aged, Infections often have atypical presentations which may complicate and delay diagnosis. The most frequently encountered atypical presentations of infections include

delirium, anorexia, functional impairment, falls, fatigue, and new or worsening urinary incontinence.^[4,5]

Moreover, the classical clinical signs of infectious diseases are usually absent in older patients, causing further diagnostic ambiguity. For instance, many older patients with acute infections have absent febrile response, chills, and leukocytosis. More frequently, infections in elderly manifest as an exacerbation of chronic stable medical illness .e.g. congestive heart failure or diabetes^[4].

Thus, health care professionals should remain alert to these atypical and subtle presentations and their associated risk factors to improve clinical outcomes when managing acute infections in elderly.

This study aimed to achieve a better understanding of the prevalence of different presenting features of the

most common infections among hospitalized medical elderly patients and to detect factors associated with the altered presentations.

Methods

The medical records of all patients with a definite diagnosis of acute community-acquired infections due to a proven focus of infection admitted to the geriatric medical ward in Ain Shams University hospital, Cairo, Egypt, between March 2017 and February 2019 were reviewed to construct a retrospective observational study.

We excluded cases referred from nursing homes. Those with nosocomial infections, asymptomatic bacteriuria, those presented with severe infections and/ or hemodynamic instability mandating critical care unit admission, cases with surgical infections, or sepsis of unrecognized source when clinical and microbiological data failed to locate any infectious focus were excluded. We excluded cases whose atypical presentations were attributed to causes other than infections like myocardial infarction, any organ failure, new medications, drug withdrawal, fecal impaction, urine retention, etc.

The following data were extracted from patients' medical records:

Age, gender, medical comorbidities, diagnoses, symptoms and signs, cognitive state [Mini mental state examination [MMSE]^[6], clinical frailty scale where degrees of 5 and above denote frailty^[7], functional status [activities of daily living [ADL]^[8] and instrumental activities of daily living [IADL]^[9], laboratory investigations [total leucocyte count, albumin, blood urea nitrogen, creatinine, C-reactive protein [CRP], Chest X-ray, and bacteriological tests [sputum, urine, blood cultures, and other site cultures as required for each case]. In-hospital mortality was also recorded.

Although, diagnosing acute infections in elderly is challenging due to altered presentations and underreporting, an accurate and detailed history and physical examination supported by invasive tests can lead to a correct diagnosis in most of the cases^[10]. Thus all cases presented with classical localizing symptoms were diagnosed according to clinical guidelines applied per hospital protocol. Any case admitted with any subtle changes or any of the symptoms suggesting atypical presentation were subjected to a systematic diagnostic approach including history, physical examination, laboratory testing (full blood count, liver and kidney functions, electrolytes, and cardiac enzymes), radiological (Chest X ray, pelvi-abdominal ultrasound, CT brain), electrocardiogram and bacteriological testing.

Definitions:

Classical presentations for common infections: included fever, chills, localizing pain, and other localizing symptoms that differed according to the type of infection.

Atypical symptoms: the presence of an unusual symptoms or signs that included delirium, functional impairment, anorexia, incontinence, and falls.^[5]

Diagnostic criteria for reported infections:

- Urinary tract infection [UTI] was diagnosed with the presence of urinary symptoms, pyuria, and the isolation of a urinary pathogen in a urine culture. Urinary symptoms include any of the following: dysuria, frequency, urgency, nocturia, hematuria, and suprapubic, loin pain]. Pyuria is the presence of leucocytes $\geq 10/ \text{mm}^3$ in a non-centrifuged urine or $\geq 5/ \text{high}$ power field in a centrifuged urine^[11]
- Diagnosis of community-acquired pneumonia [CAP] was based on: the presence of chest x-ray infiltrates on admission and one or more of symptoms and signs suggesting pneumonia e.g. cough, pleuritic chest pain, dyspnea, expectoration, rigor or night sweating]. Signs suggesting pneumonia include: tachypnea, temperature $>38^\circ \text{C}$ or $<35^\circ \text{C}$, decreased air entry, limited chest expansion, dullness on percussion, bronchial breathing, and crackles.^[12]
- Acute exacerbation of chronic obstructive pulmonary disease [AECOPD]: Major symptoms include worsening dyspnea, increased sputum volume and/or purulence, while minor symptoms include increased wheezing, worsened cough, fever, or a 20% increased breath rate or pulse.^[13]
- Uncomplicated acute bronchitis: was diagnosed upon clinical presentation, it has no reliable specific signs or laboratory tests. It was diagnosed by the presence of acute cough which can be productive for less than three weeks with or without fever, wheezing, or exertional dyspnea.^[14]
- Infectious acute gastroenteritis was diagnosed by diarrhea (≥ 3 unformed stools daily) associated with one of the following symptoms [nausea, vomiting, abdominal pain, moderate flatulence, tenesmus, fecal urgency] with or without fever for less than 14 days.^[15]
- Skin and soft tissue infections [SSTI] are diagnosed by the presence of swelling, localized pain, redness, warmth, ulceration, bullae, and /or oozing discharge.^[16]
- Infective endocarditis was diagnosed according to the modified Duke criteria.^[17]
- Acute encephalitis was diagnosed by acute altered mental status, focal neurological signs, seizures, headache, or fever. Diagnosis was

confirmed by magnetic resonance imaging and lumbar puncture.^[18]

- Septic arthritis diagnosed by localized joint pain, warmth, limited movement that was confirmed by synovial fluid white cell count > 25,000/mm³, and synovial fluid aspirate culture.^[19]

Ethical consideration:

Data were obtained by retrospective review of medical records after the study methodology was reviewed and approved by the Research Review Board of the Geriatric medicine department, Faculty of Medicine. Informed consent of participants was not required due to the retrospective study design, moreover, confidentiality and anonymity of all participants were ensured.

Statistical methods:

The extracted data were coded, tabulated, and analyzed using SPSS package 22. Quantitative variables were presented in the form of means and standard deviation or median and interquartile range as indicated. Qualitative variables were presented in the form of frequency tables [number and percent].

A comparison between quantitative variables was performed using Student t test or Mann-Whitney U. The comparison between qualitative variables was carried out using Pearson’s χ^2 test. Logistic regression model was performed to test the significant predictors for atypical presentation. Statistical difference was accepted when $p < 0.05$.

Results

The study included a total of 220 patients, females comprised 50.1% of the participants. The mean age of the study participants was 71.82±7.82 years old. 78[35.5%] of the patients presented with atypical non-specific manifestations in absence of classical ones.

In this study, UTI accounted for 44.5% of all infections, followed by community-acquired pneumonia [25.5%], and uncomplicated acute bronchitis accounting for 23.6% of cases. 25.9% of cases had more than one focus of infection recorded in their records [Table 1].

About two-thirds of the cases had an absent febrile response to their infection. The decreased oral intake was the most prevalent presenting complaint followed by unexplained new functional decline. Tachypnea and tachycardia were reported in 55.5% and 40.5% of cases, respectively [Table 1].

Table 2 showed the prevalence of different presentations for common infections in the studied sample

Table 1: Clinical characteristics of the participants:

Variables		
age		71.82±7.82
Gender	male	90(40.9%)
	female	130(50.1%)
Comorbid conditions		
DM		101(45.9%)
HTN		125(56.8%)
Cardiac diseases		103(46.8%)
Pulmonary diseases		42(19.1%)
Cerebrovascular stroke		51(23.2%)
CKD		57(25.9%)
CLD		24(10.9%)
Malignancy		2 (0.9%)
Dementia		58(26.4%)
Frailty according to clinical frailty scale(CFS)	Robust: CFS(1-3)	77(35%)
	Prefrail: CFS (4)	41(18.6%)
	Frail: CFS (5-9)	102(46.4%)
Baseline functional status	independent	62(28.2%)
	IADL dependency	20(9.1%)
	ADL dependency	52(23.6%)
	Mobility restriction	86 (39.1%)
Number of infections recorded in each patient’s chart	Single site infection	163(74.1%)
	Two or more foci of infection	57(25.9%)
Source of infection		
Urinary tract infections		98(44.5%)
community acquired Pneumonia (CAP)		56(25.5%)
skin and soft tissue infections (SSTIs)		44(20.0%)
Uncomplicated acute bronchitis		52(23.6%)
Acute exacerbation of COPD		11(5.0%)
Infectious acute gastroenteritis		10(4.6%)
Other infections		5(2.3%)
Presentation	Classical presentation	142(64.5%)
	Atypical presentation	78(35.5%)
Atypical presentations		
Blunt fever response		142(64.5%)
Delirium		73(33.2%)
Decreased oral intake		80(36.4%)
New falls		10(4.5%)
New functional decline		67(30.5%)
Worsening of chronic medical condition		
hyperglycemia		49(22.4%)
Decompensated Congestive heart failure		38(17.3%)
Decompensated Cor pulmonale		15(6.8%)
Fulminant liver cell failure		3(1.4%)
Rapid AF		9(4.1%)
Other relevant signs		
Tachypnea >20 B/m		122(55.5%)
Tachycardia>90 bpm		89(40.5%)
leukocytosis		69 (31.4%)
leukopenia		3(1.4%)

- SSTIs includes cellulitis 31(14.1%), infected pressure ulcers 11(5.0%), diabetic foot 1 (0.5%) and necrotizing Fasciitis 1(0.5%)
- Acute bronchitis 52(23.6%) of which 25 cases have acute bronchitis without any other sources of infection
- Other infections include a case of spontaneous bacterial peritonitis, one case of septic arthritis, one case of sub-acute infective endocarditis, and two cases of viral encephalitis.
- AF: atrial fibrillation, CKD: chronic kidney disease, CLD: chronic liver disease, COPD: chronic obstructive pulmonary disease, DM: Diabetes Mellitus, HTN: hypertension

Table 2: Presenting features of each infection:

Site	Presenting symptom	percentage
UTI n(%)		98(44.5%)
	Dysuric symptoms	47(48%)
	Increased or new onset incontinence	50(51%)
	Loin pain	24 (24.5%)
	fever	36 (36.7%)
	Decreased oral intake	38(38.8%)
CAP n(%)		56(25.5%)
	Cough	32(57.1%)
	Expectoration	31(55.4%)
	Fever	21(37.5%)
	Chest pain	7(12.5%)
	Dyspnea	33(58.9%)
	Delirium	21(37.5%)
	Decreased oral intake	28(50.0%)
Acute bronchitis n(%)		52(23.6%)
	Cough	52(100.0%)
	Expectoration	51(98.07%)
	Fever	17(32.69%)
	Chest pain	6(11.53%)
	Dyspnea	18(34.61%)
	Delirium	8 (15.38%)
	Decreased oral intake	17(32.69%)
AECOPD n(%)		11(5.0%)
	Cough	11(100.0%)
	Expectoration	11(100.0%)
	Fever	2(18.18%)
	Chest pain	1(9.09%)
	Dyspnea	9(81.81%)
	Delirium	0(0.0%)
	Decreased oral intake	1(9.09%)
Infected pressure ulcer n(%)		11(5.0%)
	Local pain	1(9.1%)
	erythema	4(36.4%)
	Offensive discharge	6(54.5%)
	Fever	7(63.6%)
	Delirium	9(81.8%)
	Decreased oral intake	7(63.6%)
Cellulitis n(%)		31(14.1%)
	Pain	27(87.1%)
	Erythema	31(100.0%)
	Swelling	29(93.54%)
	Hottness	31(100.0%)
	Fever	11(35.5%)
	Delirium	3(9.7%)
	Decreased oral intake	9(29%)
Infectious acute gastroenteritis n(%)	infectious diarrhea	10(4.6%)
	Abdominal pain	7(70.0%)
	Vomiting	6(60.0%)
	Fever	5(50.0%)
	Delirium	4(40.0%)
	Decreased oral intake	6(60.0%)
	Dehydration	6(60.0%)
	Electrolyte disturbance	5(50.0%)
	Fecal incontinence	3(30%)

- AECOPD: acute exacerbation of COPD
- CAP: community acquired pneumonia, UTI: urinary tract infections

Table 4: multiple logistic regression for variables associated with atypical presentation for infection in elderly:

Variable	Coefficient	Odds ratio	95% CI	P
Age	-0.007	0.99	0.94 - 1.04	0.761
Number of comorbidities	-0.719	0.48	0.33 - 0.72	0.0003*
CRP level	0.006	1.01	0.99 - 1.01	0.062
Albumin level	-0.35	0.70	0.36 - 1.38	0.304
Frailty	1.71	5.54	2.07 - 14.87	0.0007*
Dementia	1.38	4.01	1.65 - 9.73	0.002*
ADL dependency	0.37	1.45	0.51 - 4.07	0.484
Constant	0.069			0.974

- *statistical significance, ADL: activity of daily living, CRP: C reactive protein

Comparing patients with classical presentations to those with atypical presentations, revealed that those with atypical presentations were older, had less medical comorbidities, had lower albumin level, and higher CRP levels. Dementia, frailty, and ADL dependency were significantly associated with atypical presentation [Table 3].

Although mortality in our study did not exceed 5%, it was significantly higher in those with atypical presentation. The mortality included two cases presented with acute confusion [one diagnosed with infected pressure ulcer and the other case had combined UTI and acute bronchitis].

Both cases developed aspiration pneumonia and acute respiratory distress syndrome [ARDS]. Another three cases with CAP deteriorated to respiratory failure and ARDS. One case of infected pressure ulcer developed septic shock and multi-organ failure [MOF]. The case with infective endocarditis developed gentamycin related acute kidney injury requiring repeated dialysis for pulmonary edema. One case of cellulitis was rapidly progressive and was confirmed as necrotizing fasciitis, he was referred to the surgical unit, with postoperative mortality due to septic shock and MOF. One case with viral encephalitis did not respond to acyclovir.

In an adjusted model for age, CRP, albumin, and ADL dependency, the presence of dementia and frailty increased the risk of atypical presentation of infection [Table 4].

Table 3: comparison between those with classical and atypical presentations:

	Cases with classical presentation N= 142	Cases atypically presented N=78	P value
Age	70.99±7.66	73.33±7.93	0.034*
Gender			
	Males 57(40.1%)	33(42.3%)	0.75
	Females 85(59.9%)	45(57.7%)	
Number of Comorbidities	2(2)	2(1)	0.018*
Median(IQR)			
Dementia	17(12.0%)	41(52.60%)	<0.0001*
Frailty	44(31.0%)	58(74.4%)	<0.0001*
ADL dependency	74(52.1%)	64(82.1%)	<0.0001*
Albumin	3.14±0.55	2.79±0.59	<0.0001*
CRP ¶	64.71±55.64	86.98±64.38	0.014*
In hospital mortality	2(1.4%)	7(9.0%)	0.007*

- ¶ Data were available for only 193 cases
- *statistical significance
- CRP: C reactive protein

Discussion

This study was conducted to describe the presenting features of acute infections among hospitalized elderly patients in a geriatric medical ward. The inclusion of patients admitted to the geriatric ward while excluding surgical infections and those admitted to the critical care unit had particular advantages that all cases were evaluated by a multidisciplinary geriatric team and underwent comprehensive geriatric assessment.

In the current study, we found that UTI and pneumonia were the most commonly encountered infections. These findings agreed with previous literature^[20-22], moreover, we found that UTI was present as a single source of infection in 54 cases [24.5%], pneumonia was present in 40 cases [18.2%], and they both co-occurred in 12 patients [5.4%].

The coexistence of both infections was previously reported by Grabska et al.,^[23] in 7.5% of the patients with acute ischemic stroke. Similarly, Ovbiagele et al.,^[24] reported both infections simultaneously in 2.6% of the patients with acute stroke. However, both studies analyzed hospital-acquired infections. The exact prevalence of the co-occurrence of both infections in community settings could not be found in the literature.

Absent fever response to infections is common in older adults, especially frail elderly who have lower baseline temperature compared to their healthier counterparts.^[25] In this study, 142[64.5%] of the participants were afebrile. The fever in the elderly is usually defined as a rise in temperature of ≥ 1.3 °C above baseline^[26]. However; it was difficult to obtain the baseline temperature for the studied cohort from their medical records. Thus fever in the current study was defined as temperatures higher than 38 °C to detect the prevalence of a febrile response using the diagnostic cut off used for young adults.

In the current study, 114 cases presented with exacerbations of their chronic stable condition, 49 of the 101 patients with DM were presented with hyperglycemia [random blood glucose >200 mg/dl]. Hyperglycemia could be a risk factor for immunosuppression causing acute infections or a consequence of the stress caused by acute infections or withholding the usual medications during the acute illness. In the current study, 71.7% of cases with congestive heart failure presented with acute decompensation. The exact mechanisms of decompensated heart failure during acute infections are not well understood. It could be due to direct infection of the myocardium or myocardial dysfunction caused by circulating or local cytokines.^[27] Moreover, it could be attributed to the withholding therapy during acute illness.

Although uncomplicated acute bronchitis is a self-limiting disease caused by viruses in 90% of cases and does not require antibiotic therapy, 52 cases with uncomplicated acute bronchitis were hospitalized and received antibiotic therapy in our study. 27 of them had another simultaneous source of infection that justified antibiotic use [7 cases had cellulitis, 18 cases had UTI, one case had both UTI and

cellulitis, and one case was associated with infectious gastroenteritis]. Another 3 cases presented with delirium that could not be attributed to another cause. However, the remaining 23 cases accounting for 44.23% of uncomplicated acute bronchitis had unjustified antibiotic use. This was in accordance with many previous studies that reported similar unjustified use of antibiotics for acute bronchitis in the elderly^[28] and adults in general.^[29]

In the current study, the presence of dementia and frailty increased the risk for the atypical presentation in acute infections. Limpawattana et al. reported that baseline dementia was associated with atypical presentations of infections [OR 3.48, 95% CI 1.38, 8.77, $p = 0.008$]^[5], as those with cognitive impairment may be unable to describe their symptoms.

We have reported that frailty was an independent predictor of atypical presentations, it was not a surprising result. Indeed, the atypical presentation is usually considered a clinical sign of frailty.^[30] Frail elderly have decreased reserve, thus their body can't tolerate minor stressors well, leading to deterioration in different organs causing altered presentations.

Regarding mortality, about 4.1% of the cases included in the current study died during hospital admission. This mortality rate is lower than previously reported data^[31,32] because we excluded cases presenting with severe infections and/or hemodynamic instability that mandate critical care unit admission. However, despite this relatively favorable in-hospital mortality, the atypical presentation was significantly associated with higher mortality rates compared to the classical presentation [9% v.s.1.4%, $p = 0.007$], this could be explained by the delayed diagnosis and therefore antibiotic initiation.

This study had several limitations. First, this is a single center study that was performed at the only public standalone geriatric hospital in our country. Second, the study was retrospective limited to routinely collected data, time from presentation till admission was not recorded, post discharge outcome was absent. Third, collecting data of patients admitted to geriatric hospital only, this reduced the inclusion of some infections like infective endocarditis, encephalitis which are commonly admitted to other departments e.g. cardiology and neurology departments.

In conclusion, older adults present acute infections differently. Many common infections present as new functional decline, new or worsened incontinence [urine, fecal], delirium, anorexia, or falls, especially in those with dementia and frailty. Fever is usually absent in the elderly. Moreover, infections in the elderly may present as an exacerbation of chronic stable medical illness e.g. congestive heart failure or diabetes. The in-hospital mortality is higher among those having atypical presentations.

Conflicts of interest: None

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