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Burden of community acquired pneumonia in medically admitted patients with positive past admission history

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Abstract

Aims: The study examined the correlation between Community-Acquired Pneumonia (CAP) burden in hospitalized geriatric patients and their history of admission frequency, revealing a correlation between previous admissions and CAP burden in newly admitted patients.

Methods: This study analyzed geriatric patients aged 65 and above admitted to King Hussein Medical Centre in Amman, Jordan. The patients were divided into two age groups and assessed for prognostic factors such as frequency of prior admissions, CURB-65 assessment score, comorbidity burden, and composite outcomes of interest (cOI). The study found that positive cOI was associated with adverse outcomes such as high admission rates, transfers to critical care units, oxygen desaturation, and mortality. Patients were divided into two groups based on Community-Acquired Pneumonia (CAP) diagnosis, with improved cOI indicating the absence of adverse outcomes. The study conducted multiple linear regression analysis to investigate the relationship between past admission frequencies and CAP severity. The results showed significant correlations between factors such as age, gender, and comorbidity burden.

Results: This retrospective observational study evaluated 641 geriatric patients who were medically admitted for community-acquired pneumonia (CAP). The results showed that approximately 52.73% (338 patients) experienced a negative diagnosis of CAP, while 47.27% (303 patients) experienced a positive diagnosis. The study found a statistically significant difference in the tested gender between the dichotomised outcome groups (Groups I-II). The odds ratio for a positive CAP in elderly geriatric patients admitted for medical reasons was found to be 3.441. The CAP positivity group had a distribution rate for poorer outcomes of approximately 74.9% (227 patients) compared to 29.0% (98 patients) in the CAP negativity group. The study also found a statistically significant association between comorbidity burden and frailty among geriatric patients. The highest distribution rates were observed in geriatric patients with a CURB-65 score of 3, followed by those with a score of 4, with frequencies of 171 (56.4%) and 124 (40.9%), respectively. The study performed a multiple linear regression analysis, focusing on the assessment of CURB-65 scores in geriatric patients diagnosed with community-acquired pneumonia who were medically admitted. The constructed regression model accounted for approximately 86.4% of the variability in the target variable, as explained by the four independent variables tested.

Conclusion: The study found a significant correlation between geriatric patients' prior admission history and the diagnosis of community-acquired pneumonia, indicating an increased severity of CAP with a higher frequency of past admission days.

Keywords: Community acquired pneumonia; Medically admitted patients; Positive admission days

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1. Introduction

Community Acquired Pneumonia (CAP) is a significant public health issue in the community, defined as an acute infection of parenchymal lung structure that is generally associated with respiratory symptoms and an infiltrated area on the chest roentgenogram [1-2]. It includes pneumonia diagnosed upon presentation to the ED or within a short timeframe post hospitalization [3]. The global incidence rate of CAP depends on the patient population and varies from 5-11 per 1000 inhabitants to 23-40 per 1000 depending on age categorization [4]. In those over 85 years old, the incidence rates increase up to 500 per 1000. From 50% to 70% of patients with moderate to severe CAP have one or several underlying diseases [5].

CAP ranks sixth globally in terms of incidence rates but has the highest non-injury-related hospitalization rate [6]. Medically admitted patients with CAP have a secondary hospitalization rate of around 15%, which is of great relevance for public health because secondary discharges have major health care implications [7]. It requires improved handover to general practice, less uncertainty for patients and their carers about evidence-based diagnosis and evidence-based treatment, and major improvements in time-related quality of care [8].

The burden of CAP is often underestimated, as most cases are managed in the community and at residential care homes without medical assistance and hence are not recorded officially [9]. Studies within the last 25 years have shown that up to one-third of all the acutely ill medically admitted patients have had one or more admissions in the previous two years, and approximately 90% of the deaths occurring in these patients can be predicted on the basis of their age, comorbidity, and other physiological parameters at the time of the first admission [10]. Furthermore, those who had been admitted less than three months before the given admission, one or more patients in three dies [11]. Patients with CAP generally present with a several days history of cough, sputum production, pleuritic chest pain, difficulty breathing, and systemic symptoms such as fever, anorexia, headache, myalgia, and lethargy [12]. Examination can reveal crackles in the chest, a high respiratory rate with breathing through pursed lips, and the use of accessory muscles for breathing with a sat-up posture [13].

However, not all patients with CAP can present with cough, sputum, fever, or chest complaints [14]. Some may have signs and symptoms that do not seem to emanate from the lungs [15]. Diagnosis of CAP is based on a good history, physical examination, and a chest X-ray, with accurate interpretation of the results being essential for the timely commencement of therapy [16]. Timely onset of effective therapy can shorten the time of convalescence, reduce the need for hospitalization, and prevent mortality, especially in the very ill, very old, or those with associated diseases [17]. Clinicians then use clinical judgment in the interpretation of diagnostic tests and tailor therapy to the individual patient constellation of clinical findings [18].

This study primarily aimed to investigate the associations between the burden of Community-Acquired Pneumonia (CAP) in hospitalised geriatric medical patients, as indicated by CURB-65 scoring, and the patients' history of admission frequency, positing a correlation between previous admissions and the CAP burden in newly admitted geriatric patients.

2. Methods and Materials

This study is a retrospective observational study conducted on patients who were admitted to our institution, King Hussein Medical Centre at the Royal Medical Services, Amman, Jordan, between the years 2023 and May 2024. This study was initially approved by the Jordanian Royal Medical Services (JRMS) Institutional Review Board (IRB) at 15 October 2024 under the registration number of 17_15/2024. This approved study was officially permitted for publication after reviewing by our institutional directorate of professional training and planning at 4 November 2024. This study was thoroughly followed the declarations of Helsinki rules.

This study exclusively included geriatric patients (≥65 years) admitted to the medical departments of King Hussein Medical Centre at the Royal Medical Services in Amman, Jordan, comprising both females and males. The eligibility criteria for including tested patients required admission periods of at least two days and the availability of a minimum of two biochemical laboratories for analysis. This study primarily gathered patients' demographic and prognostic data. The assessed patients' demographic variables highlighted both age and gender among the elderly population.

The patients were classified into two age groups: those over 75 years and those between 65 and 75 years. The examined prognostic factors primarily encompassed the frequency of prior admissions, the CURB-65 assessment score, the comorbidity burden evaluated via the age-adjusted Charlson comorbidity index (AACCI), the frailty level as ascertained by the clinical frailty scale (CFS), and the occurrence of adverse outcomes of interest, specifically defined as composite

outcomes of interest (cOI). Significantly, the positivity of cOI was associated with several adverse outcomes, including an unexpectedly high admission rate, transfers to critical care units, oxygen desaturation in room air, and mortality.

Patients eligible for this study were primarily divided into two major comparative groups based on the diagnosis of Community-Acquired Pneumonia (CAP) after admission, assessed using the CURB-65 scoring system. Group I consisted of admitted geriatric patients without evidence of CAP diagnosis, while Group II included admitted geriatric patients with a confirmed CAP diagnosis. All variables of the previously mentioned geriatric patients were examined for variations across the CAP-related groups (Group I-II). The patients' cOI variables were dichotomised into superior or inferior cOI.

The improved cOI highlighted the absence of evidence for the occurrence of the specified adverse outcomes, while positivity required the occurrence of at least one. The frequencies of past admissions for patients in this study were classified from 0 to a maximum of nine in the geriatric patients evaluated. The assessment scoring for CAP severity in this study was classified from 1 to a maximum score of 5. Both prognostic scoring systems, the AACCI and CFS, were dichotomised into lower and higher categories based on the predefined thresholds of 7 and 5, respectively.

We conducted multiple linear regression analysis on four independent variables to investigate the relationship between the past admission frequencies of the studied patients and other potential confounders, including age, gender, and comorbidity burden, in relation to the severity of CAP as indicated by CURB-65 scoring. As a result, we obtained the regression coefficients, along with their adjusted standard errors and confidence intervals. Additionally, we evaluated the correlation strength, the variance of the dependent variable elucidated by the four specified independent variables, and the significance of the model's goodness of fit in the multiple linear regression analysis. This research utilised Microsoft Excel version 20 and IBM SPSS Statistics version 25 for the collection, filtration, revision, and analysis of patient data.

3. Results

This retrospective observational study evaluated 641 geriatric patients who were medically admitted, revealing that approximately 52.73% (338 patients) experienced a negative diagnosis of CAP, while approximately 47.27% (303 patients) experienced a positive diagnosis of CAP.

The study included 318 female and 323 male geriatric patients (49.6% and 50.4%, respectively). In this study, we found a statistically significant difference in the tested gender between the dichotomised outcome groups (Groups I-II) [p-value=0.000]. This study found that admitted geriatric males had an odd ratio for receiving a positive CAP diagnosis of 14.629 (95% CI; 9.962-21.482) compared to females. The positivity CAP distribution rate for tested males was 246 (81.2%), compared to 57 (18.8%) for tested geriatric females.

In this study, we demonstrated statistical significance between age dichotomised categories: older geriatric patients aged \geq 75 years and younger geriatric patients aged 65-74 years. The odds ratio for a positive CAP in elderly geriatric patients admitted for medical reasons compared to younger counterparts was found to be 3.441 (95% CI: 2.474-4.786). This study included approximately 56.2% (360 patients) aged 75 years or older and approximately 43.8% (281 patients) aged less than 75 years. In fact, the positive CAP group (Group II) included approximately 71.6% (217 patients) of elderly geriatric patients, compared to 28.4% (86 patients) of younger geriatric patients.

This study found a statistically significant difference between CAP-based comparison groups (CAP negativity group or Group I versus CAP positivity group or Group II), with an estimated propensity for lower cOI of 7.315 (95% CI; 5.153-10.383) in the CAP positivity group compared to the CAP negativity group. Nonetheless, the CAP positivity group had a distribution rate for poorer outcomes of approximately 74.9% (227 patients) as opposed to approximately 29.0% (98 patients) in the CAP negativity group.

After analysing the differences in past admission frequencies among the tested geriatric patients, we discovered a statistically significant difference between the CAP negativity and CAP positivity groups. The highest distribution rates for geriatric patients in our study were recorded for three previous admissions, followed by four, with 104 (16.2%) and 99 (15.4%), respectively. Nonetheless, the CAP negativity cohort had the highest distribution rates among geriatric patients, with three prior admissions, followed by two, at 93 (27.5%) and 86 (25.4%), respectively. Conversely, the CAP positivity group had the highest distribution rates among geriatric patients, with prior admission frequencies of seven and six times, recorded at 91 (30.0%) and 77 (25.4%), respectively.

Upon evaluating the geriatric patients, we observed a statistically significant association between comorbidity burden, as indicated by the AACCI with a threshold of 7, and frailty, as measured by the CFS with a threshold of 5. This study indicated an unadjusted propensity estimate for CAP positivity upon admission in geriatric medical departments of 82.265 (95% CI; 33.118-204.342) for patients with an AACCI score of \geq 7, compared to those with a baseline AACCI score of <7. This study revealed an unadjusted propensity for experiencing CAP positivity among geriatric patients upon admission, quantified at 316.642 (95% CI; 43.948-2281.367), when their assessed CFS score surpassed the threshold of 5. In this study, the CAP positivity group exhibited distribution rates of 298 (98.3%) and 302 (99.7%), in contrast to the CAP negativity group, which had distribution rates of 142 (42.0%) and 165 (48.8%) among geriatric admission patients with AACCI and CFS scores of \geq 7 and \geq 5, respectively.

Nonetheless. This study assessed the CURB-65 score in geriatric patients upon admission for community-acquired pneumonia (CAP), revealing statistically significant distribution rates. The highest distribution rate was observed in geriatric patients with a CURB-65 score of 3, followed by those with a score of 4, with frequencies of 171 (56.4%) and 124 (40.9%), respectively. The geriatric patients admitted, whose clinical diagnosis did not indicate a CAP diagnosis, exhibited an assessed CURB-65 score ranging from 1 to 2 in this study. The results of the comparative analyses of geriatric patients across the dichotomised groups of admitted patients with CAP are fully detailed in Table 1 below.

	Negative CAP	Positive CAP	Overall	OD	P-Value	
	(338, 52.73%)	(303, 47.27%)	641			
Gender		•				
F	261 (77.2%)	57 (18.8%)	318 (49.6%)	14.629	0.000	
М	77 (22.8%)	246 (81.2%)	323 (50.4%)	(95% CI; 9.962-21.482)		
Age (Years)					·	
<75	195 (57.7%)	86 (28.4%)	281 (43.8%)	3.441	0.000	
≥75	143 (42.3%)	217 (71.6%)	360 (56.2%)	(95% CI; 2.474-4.786)		
cOI						
Better	240 (71.0%)	76 (25.1%)	316 (49.3%)	7.315	0.000	
Poorer	98 (29.0%)	227 (74.9%)	325 (50.7%)	(95% CI; 5.153-10.383)		
Past Admission x						
0	8 (2.4%)	0 (0.0%)	8 (1.2%)	NA	0.000	
1	31 (9.2%)	0 (0.0%)	31 (4.8%)			
2	86 (25.4%)	0 (0.0%)	86 (13.4%)			
3	93 (27.5%)	11 (3.6%)	104 (16.2%)			
4	52 (15.4%)	47 (15.5%)	99 (15.4%)			
5	54 (16.0%)	34 (11.2%)	88 (13.7%)			
6	14 (4.1%)	77 (25.4%)	91 (14.2%)			
7	0 (0.0%)	91 (30.0%)	91 (14.2%)			
8	0 (0.0%)	35 (11.6%)	35 (5.5%)			
9	0 (0.0%)	8 (2.6%)	8 (1.2%)			
CURB_65						
1	43 (12.7%)	0 (0.0%)	43 (6.7%)	NA	0.000	
2	295 (87.3%)	0 (0.0%)	295 (46.0%)			

Table 1 Patients' comparative tested variables across CAP negativity group (Group I) and CAP positivity group (Group II)

3	0 (0.0%)	171 (56.4%)	171 (26.7%)			
4	0 (0.0%)	124 (40.9%)	124 (19.3%)			
5	0 (0.0%)	8 (2.6%)	8 (1.2%)			
AACCI						
<7	196 (58.0%)	5 (1.7%)	201 (31.4%)	82.265	0.000	
≥7	142 (42.0%)	298 (98.3%)	440 (68.6%)	(95% CI; 33.118- 204.342)		
CFS						
<5	173 (51.2%)	1 (0.3%)	174 (27.1%)	316.642	0.000	
≥5	165 (48.8%)	302 (99.7%)	467 (72.9%)	(95% CI; 43.948- 2281.367)		
two groups: pat	ients with negative ev ady indicated a higher	vidence of CAP (Group	I) and patients	n rates of various tested vari with a positive diagnosis of fers to critical units, oxygen o	CAP (Group	
CAP: Community	y acquired pneumonia	а.	AACCI: Age adj	usted charlson comorbidity	index.	
CURR65: Score for CAP encounters confusion blood urea			CFS" Clinical frailty score			

diff i dominiantly acquired pricationial	Three a gabted charibon comorbianty machi
CURB65: Score for CAP encounters confusion, blood urea	
nitrogen respiratory rate, blood pressure, and age \geq 65	cOI: Composited outcomes of interest.
years.	F & M: Genders, females and males.

This study performed a multiple linear regression analysis, focusing on the assessment of CURB-65 scores in geriatric patients diagnosed with community-acquired pneumonia who were medically admitted. This study primarily utilised patients' past admission frequencies as the main independent variable, while additionally considering potential confounders such as the ages, genders, and comorbidity burdens of geriatric patients, as indicated by the AACCI. Our study demonstrated statistical significance for all four independent variables in estimating the CURB-65 scores of admitted geriatric patients with community-acquired pneumonia (CAP), yielding a correlation (R) of 0.930 among age, gender, past admission frequency, and comorbidity burden in relation to the assessed CURB-65 scores. The constructed regression model accounted for approximately 86.4% of the variability (R2) in the target variable, as explained by the four independent variables tested. The adjusted goodness of fit was maintained at a high level of 0.864 with the four independent variables tested. The ANOVA table indicated a statistically significant result for the constructed regression model [F (4, 115.047) = 1013.428, p-value = 0.000] compared to merely predicting the mean of the dependent variable. Our study demonstrated a regression coefficient of 0.349±0.014 (95% CI; 0.322-0.375) for each prior admission in relation to CURB-65 incremental scoring. The chi-square analysis previously indicated a positive statistically significant regression correlation of 0.008±0.003 (95% CI; 0.002-0.014) for each year concerning the incremental CURB-65 scores of tested patients in this multiple linear regression analysis. The multiple linear regression analysis for the four independent variables concerning the patients' CUIRB65 scores is presented in Table 2 below.

Table 2 Multiple linear regression analysis for the four examined independent variables in relation to the patients'CUIRB65 score

Model	Unstandardized Coefficients	Standardized Coefficients	t	Sig.	95.% CI B	
	B±SE	Beta			LL	UL
(Constant)	0.852± 0.188		4.541	0.000	0.484	1.221
Past Amission #	0.349±0.014	0.789	25.568	0.000	0.322	0.375
Age	0.008±0.003	0.054	2.669	0.008	0.002	0.014
Gender	0.916±0.067	0.502	13.619	0.000	0.784	1.048
AACCI	-0.122±0.040	-0.166	-3.019	0.003	-0.201	-0.043

This multiple linear regression model revealed in this study a correlation (R) of 0.930 for the four tested independent variables; age, gender, past admission frequency, and the patients' comorbidity burden, versus the assessed patients' CURB65 score. Additionally, this constructed regressional model revealed approximately 86.4% of the variability observed (R2) in the target variable which was explained by the four tested independent variables. The corrected goodness of fit was mainlined high at 0.864 with the tested four independent variables. The ANOVA table revealed a statistically significant for the constructed regressional model [F (4, 115.047) =1013.428, p-value=0.000] over just predicting the mean of the dependent variable.

AACCI: Age adjusted charlson comorbidity index.	#: Frequency.	
B: Regressional coefficient.	LL: Lower interval limit.	
SE: Standard of error.	UL: Upper interval limit.	
CI: Confidence intervals		

4. Discussion

Community-acquired pneumonia (CAP) is a significant health concern that can lead to increased morbidity and mortality in medically admitted individuals [19]. The majority of these patients are likely to have multiple conditions that may contribute to CAP, and the capacity to identify CAP from a background noise of chronic symptoms is unclear [20]. Estimates of the impact of CAP range from prolonging the average admission by 2 to 8 days [21]. The healthcare burden associated with CAP comprises a multimillion-pound cost of managing the condition, along with opportunity costs such as bed congestion and increased workload [22]. Prompting earlier interventions in this population would help establish a likely definitive diagnosis and guide subsequent therapy [23].

Some comorbid conditions that raise the risk of CAP are chronic conditions such as chronic obstructive pulmonary disease (COPD) [24]. A diagnosis of CAP when a patient also has a chronic condition complicates effective management of both conditions, as neither condition will fully and rapidly respond to treatment until both are addressed [25]. Clinical guidelines for both conditions are currently being developed [26]. It is not known whether medically admitted patients with an unrecognized past history of admission have an absolute or relative increased risk of CAP [27]. Over half of this population admitted under the care of our physicians required intravenous antibiotics in the first 72 hours, reflecting concern for acute clinical deterioration and/or a possible bacterial focus [28]. Given the clinical risks associated with severe infection in this population, this is a high-risk, high-volume area of clinical need [29].

Numerous studies and meta-analyses reported a strong association between the number of previous admissions and community-acquired pneumonia (CAP) in the preceding year [30]. Hospitalized CAP patients receiving mechanical ventilation within 48 hours of admission and the need for inotropes were both associated with significantly increasing odds of readmission compared to those who were admitted to the ward [31]. Many of them had past admissions more than double [32]. Frequently admitted patients are characterized by more comorbidities, which could be compounded by their frequent exposure to multidrug-resistant microorganisms during hospitalization and institutionalization, making them vulnerable again to acquire pneumonia [33]. A retrospective review of community-acquired pneumonia (CAP) in patients with multiple admissions concluded that for each new hospitalization episode, the readmitted patient presented an independent risk of acquiring community-acquired pneumonia [34].

This study revealed a statistically significant correlation between the frequencies of past admissions of medically admitted geriatric patients and the incidence of community-acquired pneumonia during hospitalisation. Our developed multiple linear regression model indicates that the CURB-65 score, the standard measure for CAP severity, was statistically elevated by a regression coefficient of 0.349 ± 0.014 . Additionally, consistent with prior studies, we demonstrated that both ageing and male gender were statistically significant factors associated with elevated CURB-65 scores in geriatric patients with community-acquired pneumonia (CAP), with estimated regression coefficients of 0.008±0.003 for each additional year of age and 0.916±0.067 for male patients compared to female patients. Contrary to numerous prior studies, our multiple linear regression model unexpectedly demonstrated a statistically significant negative association between baseline comorbidity burden, as indicated by the AACCI, and the severity of admitted geriatric community-acquired pneumonia (CAP), as reflected by elevated CURB-65 scores. This unexpected result may be partially explained by the presence of significant potential confounders from previous admission frequencies that may overlook the proposed positive impact of geriatric patients' comorbidity burden on the assessment of CAP severity. This study revealed a statistically significant unadjusted risk estimate for CAP positivity in geriatric patients with a baseline AACCI of \geq 7, quantified at 82.265 (95% CI; 33.118-204.342). This study is limited by its retrospective and single-center design. Our institution is a prominent tertiary centre in our country and the Middle East. This study provides valuable evidence for evaluating the correlation between past admission frequency and the positivity of community-acquired pneumonia (CAP) diagnosis, as well as assessing its severity by estimating the CURB-65 score based on multiple potentially impactful factors. A prospective randomised study is necessary to assess the causal relationship while minimising the likelihood of biases inherent in retrospective studies.

5. Conclusion

This study demonstrated a statistically significant correlation between the prior admission history of medically admitted geriatric patients and the positivity for a diagnosis of community-acquired pneumonia (CAP), suggesting an increased severity of CAP with a higher frequency of past admission days. Clinical management of CAP in patients with underlying diseases and a positive past admission history must be approached from a multidisciplinary perspective. It is important to educate patients about the disease and encourage preventive management, including vaccination, to reduce susceptibility to infection.

Compliance with ethical standards

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Disclosure of conflict of interest

There is no conflict of interest in this manuscript.

Statement of ethical approval

There is no animal/human subject involvement in this manuscript

Statement of informed consent

Owing to the retrospective design of this study, the informed consent form was waived.

References

- [1] Eshwara VK, Mukhopadhyay C, Rello J. Community-acquired bacterial pneumonia in adults: An update. Indian Journal of Medical Research. 2020 Apr 1;151(4):287-302.
- [2] Angus DC, Berry S, Lewis RJ, et al. The REMAP-CAP (randomized embedded multifactorial adaptive platform for community-acquired pneumonia) study. Rationale and design. Annals of the American Thoracic Society. 2020 Jul;17(7):879-91.
- [3] Williams DJ, Creech CB, Walter EB, et al. Short-vs standard-course outpatient antibiotic therapy for communityacquired pneumonia in children: the SCOUT-CAP randomized clinical trial. JAMA pediatrics. 2022 Mar 1;176(3):253-61.
- [4] Martin-Loeches I, Torres A, Nagavci B, Aliberti S, et al. ERS/ESICM/ESCMID/ALAT guidelines for the management of severe community-acquired pneumonia. Intensive care medicine. 2023 Jun;49(6):615-32.
- [5] Qu J, Zhang J, Chen Y, et al. Aetiology of severe community acquired pneumonia in adults identified by combined detection methods: a multi-centre prospective study in China. Emerging microbes & infections. 2022 Dec 31;11(1):556-66.
- [6] Ampuero S, Bahamonde G, Tempio F, et al. IL-7/IL7R axis dysfunction in adults with severe community-acquired pneumonia (CAP): a cross-sectional study. Scientific Reports. 2022 Jul 30;12(1):13145.
- [7] Divino V, Schranz J, Early M, et al. The annual economic burden among patients hospitalized for communityacquired pneumonia (CAP): a retrospective US cohort study. Current Medical Research and Opinion. 2020 Jan 2;36(1):151-60.
- [8] Sun Y, Li H, Pei Z, et al. Incidence of community-acquired pneumonia in urban China: a national population-based study. Vaccine. 2020 Dec 14;38(52):8362-70.

- [9] Molina J, González-Gamarra A, Ginel L, et al. Cappric study—characterization of community-acquired pneumonia in spanish adults managed in primary care settings. Microorganisms. 2021 Feb 28;9(3):508.
- [10] Duszynska W, Idziak M, Smardz K, et al. Frequency, Etiology, Mortality, Cost, and Prevention of Respiratory Tract Infections—Prospective, One Center Study. Journal of Clinical Medicine. 2022 Jun 29;11(13):3764.
- [11] Antunes C, Pereira M, Rodrigues L, et al. Hospitalization direct cost of adults with community-acquired pneumonia in Portugal from 2000 to 2009. Pulmonology. 2020 Sep 1;26(5):264-7.
- [12] McLaughlin JM, Khan FL, Thoburn EA, et al. Rates of hospitalization for community-acquired pneumonia among US adults: a systematic review. Vaccine. 2020 Jan 22;38(4):741-51.
- [13] Glöckner V, Pletz MW, Rohde G, et al. Early post-discharge mortality in CAP: frequency, risk factors and a prediction tool. European Journal of Clinical Microbiology & Infectious Diseases. 2022 Apr;41(4):621-30.
- [14] Bordon J, Slomka M, Gupta R, et al, University of Louisville Pneumonia Study Group. Hospitalization due to community-acquired pneumonia in patients with chronic obstructive pulmonary disease: incidence, epidemiology and outcomes. Clinical microbiology and infection. 2020 Feb 1;26(2):220-6.
- [15] Campling J, Wright HF, Hall GC, et al. Hospitalization costs of adult community-acquired pneumonia in England. Journal of Medical Economics. 2022 Dec 31;25(1):912-8.
- [16] Marziliano A, Burns E, Chauhan L, et al. Patient factors and hospital outcomes associated with atypical presentation in hospitalized older adults with COVID-19 during the first surge of the pandemic. The Journals of Gerontology: Series A. 2022 Apr 1;77(4):e124-32.
- [17] Rasheedy D. Atypical presentations of acute infections in hospitalized older adults: The Prevalence, Predictors, and Outcomes. The Egyptian Journal of Geriatrics and Gerontology. 2021 Oct 1;8(2):8-13.
- [18] Pop-Vicas A, Haleem A, Osman F, et al. Risk factors and mortality for atypical presentation of COVID-19 infection in hospitalized patients-lessons from the early pandemic. Wmj. 2021 Jul 1;120(2):94-9.
- [19] van Son JE, Kahn EC, van der Bol JM, et al. Atypical presentation of COVID-19 in older patients is associated with frailty but not with adverse outcomes. European Geriatric Medicine. 2023 Apr;14(2):333-43.
- [20] de Candia P, Prattichizzo F, Garavelli S, et al, Matarese G. Effect of time and titer in convalescent plasma therapy for COVID-19. IScience. 2021 Aug 20;24(8).
- [21] Klassen SA, Senefeld JW, Senese KA, et al. Convalescent plasma therapy for COVID-19: a graphical mosaic of the worldwide evidence. Frontiers in Medicine. 2021 Jun 7;8:684151.
- [22] Fernández-Lázaro D, Ortega CD, Sánchez-Serrano N, et al. Convalescent plasma therapy, therapeutic formulations of repurposed drugs in 20th century epidemics against COVID-19: a systematic review. Pharmaceutics. 2022 May 9;14(5):1020.
- [23] Bongarts Lebbe T, Rey-Valette H, Chaumillon É, et al. Designing coastal adaptation strategies to tackle sea level rise. Frontiers in Marine Science. 2021 Nov 3;8:740602.
- [24] Gavazzi G, Drevet S, Debray M, et al. Procalcitonin to reduce exposure to antibiotics and individualise treatment in hospitalised old patients with pneumonia: a randomised study. BMC geriatrics. 2022 Dec 14;22(1):965.
- [25] Butler AM, Durkin MJ, Keller MR, et al. Risk of antibiotic treatment failure in premenopausal women with uncomplicated urinary tract infection. Pharmacoepidemiology and drug safety. 2021 Oct;30(10):1360-70.
- [26] Taylor SP, Weissman GE, Kowalkowski M, et al. A quantitative study of decision thresholds for initiation of antibiotics in suspected sepsis. Medical Decision Making. 2023 Feb;43(2):175-82.
- [27] Angus DC, Derde L, Al-Beidh F, et al. Effect of hydrocortisone on mortality and organ support in patients with severe COVID-19: the REMAP-CAP COVID-19 corticosteroid domain randomized clinical trial. Jama. 2020 Oct 6;324(13):1317-29.
- [28] Singh S, Chakravarty T, Chen P, Akhmerov et al. Allogeneic cardiosphere-derived cells (CAP-1002) in critically ill COVID-19 patients: compassionate-use case series. Basic research in cardiology. 2020 Jul;115:1-1.
- [29] Salanova V, Sperling MR, Gross RE, et al. The SANTÉ study at 10 years of follow-up: effectiveness, safety, and sudden unexpected death in epilepsy. Epilepsia. 2021 Jun;62(6):1306-17.

- [30] Cheng H, Zong L, Kong Y, et al. Camrelizumab plus apatinib in patients with high-risk chemorefractory or relapsed gestational trophoblastic neoplasia (CAP 01): a single-arm, open-label, phase 2 trial. The Lancet Oncology. 2021 Nov 1;22(11):1609-17.
- [31] Fésüs A, Benkő R, Matuz M, et al. Impact of guideline adherence on outcomes in patients hospitalized with community-acquired pneumonia (CAP) in Hungary: a retrospective observational study. Antibiotics. 2022 Mar 30;11(4):468.
- [32] Dupuis C, Sabra A, Patrier J, et al. Burden of pneumococcal pneumonia requiring ICU admission in France: 1-year prognosis, resources use, and costs. Critical Care. 2021 Dec;25:1-0.
- [33] Niu Y, Xing Y, Li J, et al. Effect of community-acquired pneumonia on acute exacerbation of chronic obstructive pulmonary disease. COPD: Journal of Chronic Obstructive Pulmonary Disease. 2021 Jul 4;18(4):417-24.
- [34] 4Bielicki JA, Stöhr W, Barratt S, et al. Effect of amoxicillin dose and treatment duration on the need for antibiotic re-treatment in children with community-acquired pneumonia: the CAP-IT randomized clinical trial. Jama. 2021 Nov 2;326(17):1713-24.