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Biomarkers and clinical features associated with pressure injury among geriatric patients

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ABSTRACT

Purpose: The study aims to identify biomarkers and clinical features associated with pressure injury (PI) among geriatric patients.

Methods: A cross-sectional study including 191 patients aged ≥60 years. Patients were classified into those with and without PI. Assessing the risk of PI was performed on admission by applying the Braden scale (BS) for predicting pressure sore risk. Clinical history, baseline hematology, and biochemistry results were obtained. C-reactive protein to albumin ratio (CAR) and Charlson comorbidity index (CCI) were calculated. Statistical analyses were performed.

Results: 43 (22.5%) patients had PI. PI was significantly associated with higher CCI, total leukocyte count, and CAR, besides lower BS scores, serum albumin, and total proteins. Significant comorbidities were diabetes mellitus, stroke/transient ischemic attack, dementia, incontinence, and chronic kidney disease. The optimal cut-offs for PI occurrence were ≤14, ≤3.1 g/dl and >1.27 for BS, albumin, and CAR, respectively.

Keywords: Braden scale, older adults, pressure Injury

INTRODUCTION

As a result of the increasing longevity, besides functional and cognitive impairments, pressure injury (PI) became a concern among older adults [1]. PI represented 3.17 million incident cases and 0.85 million prevalent cases in 2019, with a prominent burden, especially among persons aged ≥95 years old [2]. PI, also known as a pressure ulcer or bedsore, represents an area of skin and soft tissue damage due to pressure and shear forces at bony prominences such as sacrum, elbows, and heels [3, 4]. PI is related to poor quality of life and higher mortality [5]. Assessment of PI risk includes several scales as Waterlow and the Braden scale (BS), both of which have high sensitivity for PI [6]. BS assesses several risk factors commonly involved in frailty assessment, such as functional, cognitive, and nutritional status [7]. These factors frequently work together in the development of PI [8].

Risk factors associated with PI include older age, low body mass index <18.5, low albumin and hemoglobin levels and high C-reactive protein (CRP) levels [9, 10]. Recently, C-reactive protein to albumin ratio (CAR) was a novel inflammatory marker in various infectious diseases and a mortality indicator in different cancers [11]. Evidence-based knowledge about factors associated with PI is crucial to mitigate the occurrence of PI in healthcare settings [9]. The study aims to identify biomarkers and clinical features associated with PI and assess the potential role of CAR in PI among geriatric patients.

METHODS

Study Design, Sitting, and Eligibility Criteria

A cross-sectional study of older patients hospitalized at the geriatrics hospital at Ain Shams University, Egypt. Geriatrics hospital is a tertiary care hospital specializing in the acute management of older patients with acute medical conditions. The inclusion criteria included all older patients (aged ≥60 years) admitted at the geriatrics hospital involving inpatient wards, intermediate care unit, and intensive care unit from April to July 2022. These patients provided informed consent before they participated in the study. Exclusion criteria included those who refused participation in the study.

Demographic, Clinical, and Laboratory Data Collection

Each patient was subjected to a detailed history taking to identify demographic data such as age, sex, and clinical data as chronic diseases and geriatric syndromes. Charlson comorbidity index (CCI) had calculated accordingly [12]. The physical examination determined the presence of PI on admission. PI is localized skin damage mostly over a bony prominence, ranging from fixed erythema (stage 1) to partial skin loss represented as a superficial ulcer or blister (stage 2) and full-thickness skin loss with exposure of subcutaneous fat (stage 3) or full-thickness skin loss with exposure of the

Table 1. Participant's characteristics and their associations with pressure injury

Qualitative variables		PI		Chi-square test (χ^2)		
		No: 148 (77.5%)	Yes: 43 (22.5%)			
		n (%)	n (%)	X^2	p-value	Significance
Sex	Female	87 (76.32%)	27 (23.68%)	0.22	0.637	Non-significant
	Male	61 (79.22%)	16 (20.78%)			
Hypertension	No	59 (83.1%)	12 (16.9%)	2.04	0.153	Non-significant
	Yes	89 (74.17%)	31 (25.83%)			
Diabetes mellitus	No	89 (83.96%)	17 (16.04%)	5.73	0.017	Significant
	Yes	59 (69.41%)	26 (30.59%)			
Chronic hepatic disease	No	112 (76.19%)	35 (23.81%)	0.62	0.433	Non-significant
	Yes	36 (81.82%)	8 (18.18%)			
Chronic kidney disease	No	113 (74.34%)	39 (25.66%)	4.22	0.040	Significant
	Yes	35 (89.74%)	4 (10.26%)			
Prostatism	No	127 (76.05%)	40 (23.95%)	1.58	0.209	Non-significant
	Yes	21 (87.5%)	3 (12.5%)			
Malignancy	No	128 (79.01%)	34 (20.99%)	1.42	0.233	Non-significant
	Yes	20 (68.97%)	9 (31.03%)			
Old stoke/transient ischemic attack	No	123 (81.46%)	28 (18.54%)	6.51	0.011	Significant
	Yes	25 (62.5%)	15 (37.5%)			
Cardiac disease	No	91 (77.78%)	26 (22.22%)	0.02	0.904	Non-significant
	Yes	57 (77.03%)	17 (22.97%)			
Chronic pulmonary disease	No	122 (75.31%)	40 (24.69%)	2.9	0.088	Non-significant
	Yes	26 (89.66%)	3 (10.34%)			
Dementia	No	117 (84.78%)	21 (15.22%)	11.34	0.001	Significant
	Yes	20 (58.82%)	14 (41.18%)			
Incontinence (urinary/faecal)	No	95 (89.62%)	11 (10.38%)	Fisher exact test	0.001	Significant
	Yes	18 (62.07%)	11 (37.93%)			

underlying structures including muscle, tendons, and bone (stage 4). Unstageable PI is characterized by slough or eschar, while deep tissue injury is a localized area of discolored intact skin in purple or blood-filled bulbous lesion because of pressure and shear force-induced damage [13]. Accordingly, all patients were classified into two groups: those with and without PI. BS was used to determine the PI risk [14]. BS includes six subscales; nutritional condition, sensory perception, skin moisture, activity, friction/shear, and mobility [14], each subscale scores from 1-4 according to the degree of limitation related to each respective risk factor. Summation of the total points resulted in a score ranging from 6-23, indicating the overall risk of PI. Lower scores of BS reflect a higher risk of PI [14, 15].

Laboratory data included results of complete blood count (CBC), CRP, blood urea nitrogen (BUN), creatinine, electrolytes, aspartate aminotransferase (AST), alanine aminotransferase (ALT), total bilirubin (TB), and total proteins (TPs) obtained from the central laboratories of Ain Shams University hospitals. CAR was calculated by dividing CRP mg/l by albumin g/l [11].

Statistical Analysis

The descriptive statistics were given as numbers and percentages for non-numerical variables and as means and standard deviations (±SD) for the numerical variables. The Chi-square test assessed the relationship between two qualitative variables. The unpaired student's t-test compared the means of the two study groups. A p-value <0.05 was the cut-off of statistical significance. The Pearson correlation measured the strength of associations; "r" defined the strength and direction (positive or negative) of the linear relationship between selected variables and BS scores (r≤0.19 is a very weak correlation, r 0.2-0.39 is a weak correlation and r≥0.6 is a strong correlation). The receiver operating characteristic (ROC) curve tested the diagnostic validity of variables. Analysis was performed by statistical package for social science (SPSS, version 25).

RESULTS

The study included 191 geriatric patients with a mean age of 73.46±8.31 years. 43 (22.5%) patients had PI on admission. The mean BS of participants was 15.59±3.84. The two groups were compared as regards demographic, clinical and laboratory variables. Particular comorbidities such as diabetes mellitus (DM), chronic kidney disease (CKD), old stroke/transient ischemic attack (TIA), dementia, and urinary/faecal incontinence were significantly associated with having PI on admission. There were also statistically significant differences regarding mean values of the BS, CCI, total leukocyte count (TLC), CAR, serum albumin and TPs (**Table 1** and **Table 2**).

Correlation analysis revealed the linear relation between BS and different variables involving CCI, CRP, albumin, and CAR. It showed a weak positive correlation between the BS and

Table 2. Participant's characteristics and their associations with pressure injury

Quantitative variables	PI		Student's t-test		
	No: 148 (77.5%)	Yes: 43 (22.5%)			
	Mean±SD	Mean±SD	t-value	p-value	Significance
Age	73.09±8.35	74.72±8.13	-1.14	0.257	Non-significant
Braden scale	16.53±3.6	12.35±2.72	8.19	<0.001	Significant
CCI	5.98±2.04	6.97±2.21	-2.54	0.012	Significant

Table 2 (Continued). Participant's characteristics and their associations with pressure injury

Quantitative variables	PI		Student's t-test		
	No: 148 (77.5%)	Yes: 43 (22.5%)			
	Mean±SD	Mean±SD	t-value	p-value	Significance
TLC	8.89±4.4	10.93±4.19	-2.67	0.008	Significant
Hemoglobin	10.55±2.62	10.04±2.24	1.13	0.258	Non-significant
Platelets	253.91±120.65	248.29±131.75	0.26	0.797	Non-significant
CRP	63.23±74.86	89.47±74.14	-1.87	0.063	Non-significant
Albumin	3.27±0.63	2.77±0.57	4.56	0.000	Significant
CAR	2.14±2.75	3.48±3.06	-2.49	0.014	Significant
BUN	36.82±32.66	39.08±24.08	-0.40	0.692	Non-significant
Creatinine	1.77±2.06	1.45±1.09	0.98	0.327	Non-significant
Sodium	136.52±5.91	137.09±8.4	-0.42	0.677	Non-significant
Potassium	4.19±0.76	4.14±0.81	0.37	0.711	Non-significant
Magnesium	1.93±0.44	1.92±0.4	0.16	0.874	Non-significant
Phosphorus	3.4±1.02	3.4±1.46	0.01	0.992	Non-significant
AST	32.88±34.45	38.12±36.74	-0.84	0.401	Non-significant
ALT	24.95±32.37	24.63±19.38	0.06	0.953	Non-significant
Total bilirubin	1.14±1.84	0.9±0.79	0.75	0.452	Non-significant
TPs	6.47±0.87	6.03±0.73	2.16	0.034	Significant

Note. CCI: Charlson comorbidity index; TLC: Total leucocyte count; CRP: C-reactive protein; CAR: C-reactive protein/albumin ratio; BUN: Blood urea nitrogen; AST: Aspartate aminotransferase; ALT: Alanine aminotransferase; TPs: Total proteins; & **Normal range** of TLC (4-10×10^3/µL), Hemoglobin (12-15 g/dl), Platelets (150-410×10^3/µL), CRP (<6mg/l), Albumin (3.5-5.7 g/dl), BUN (5-23 mg/dl), Creatinine (0.6-1.2 mg/dl), Sodium (136-145 Mmol/l), Potassium (3.5-5.1 Mmol/l), Magnesium (1.8-2.6 mg/dl), Phosphorus (2.5-5 mg/dl), AST (3-35 IU/L), ALT (7-52 IU/L), Total bilirubin (0.3-1 mg/dl), & TPs (6-8.3 g/dl).

Table 3. Correlation between the Braden scale and selected variables

Whole sample		CCI	CRP	Albumin	CAR
Braden scale	r	-0.164	-0.166	0.319	-0.194
	p-value	**0.034**	**0.036**	**<0.001**	**0.018**

Note. **Bold** numbers mean significant; CCI: Charlson comorbidity index; CRP: C-reactive protein; & CAR: C-reactive protein/albumin ratio

Table 4. Diagnostic abilities of Braden scale, serum albumin, and CRP/albumin ratio for pressure injury

Variable	AUC	95% CI	p-value	Cut-off point	Sensitivity	Specificity	PPV	NPV
Braden scale	0.820	0.758-0.872	**<0.0001**	≤14.00	86.05	73.65	48.7	94.8
Albumin	0.753	0.682-0.815	**<0.0001**	≤3.10	87.80	60.90	40.9	94.2
CAR	0.674	0.592-0.748	**0.0003**	>1.27	78.38	53.57	35.8	88.2

Note. **Bold** numbers mean significant; AUC: Area under the curve; CAR: C-reactive protein/albumin ratio; 95% CI: 95% confidence interval; PPV: Positive predictive value; & NPV: Negative predictive value

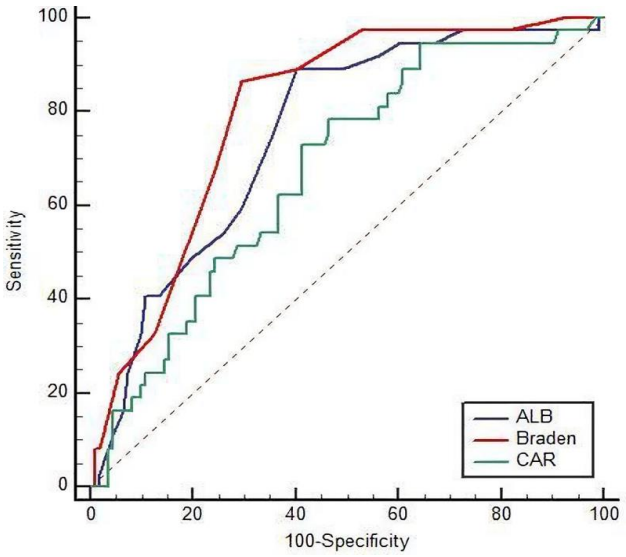

Figure 1. ROC of BS, serum albumin, and CRP/albumin ratio (Source: Authors' own elaboration)

serum albumin level (r 0.319, p-value <0.001) and a negative correlation with CCI, CRP, and CAR. The positive correlation suggested that higher serum albumin levels correlate with higher BS scores, which predict a lower risk of PI (**Table 3**).

ROC curve showed the diagnostic utility of the BS, serum albumin, and CAR for PI with the provision of an optimal cut-off values, sensitivity, and specificity of each variable. At a cut-off ≤14, BS had sensitivity of 86.05 %, and specificity of 73.65% with an area under curve (AUC) of 0.82 (95% CI: 0.758-0.872, p-value <0.0001) as described in (**Table 4** and **Figure 1**).

DISCUSSION

Skin inspection and risk assessment on hospital admission could document PI and guide proactive strategies towards PI management involving repositioning, skin care and the use of appropriate support surfaces [16, 17]. Targeting particular biomarkers and clinical features associated with PI could markedly mitigate the occurrence or progression of PI during hospitalization.

The study showed the scores of BS ≤14, serum albumin ≤3.1 g/dl, and CAR >1.27 as the optimal cut-offs for PI occurrence, their respective values of sensitivity were (86.05%, 87.8%, and 78.38%) and specificity (73.65%, 60.9%, and 53.57%). These data markedly coincide with a recent meta-analysis that

reported a pooled sensitivity of 78 % (95% CI: 0.74-0.82) and specificity of 72 % (95% CI: 0.66-0.78) with a reported AUC of 0.82 for the BS [18]. BS has shown better suitability for younger (<60 years) and hospitalized patients and has various cut-off values among different populations [18]. So, determining an optimal cut-off among older adults is of clinical benefit [18]. Previous studies provided a cut-off ≤18 to identify at-risk persons and recommended its administration upon institutionalization, every week for four weeks and with any change in the person's medical condition [15]. The present study provided a cut-off for serum albumin at ≤3.1 g/dl, similar to a previous study where serum albumin <3.1 g/dl was a predictor of PI onset and associated with malnutrition [19]. Overall, 43 (22.5%) patients had PI at the time of hospital admission. The high prevalence of community-acquired PI highlights the burden of PI and the eminent need to mitigate its occurrence or progression during hospitalization. Coinciding with another prospective study among 1,047 functionally impaired geriatric patients, it showed that 113 (10.8%) participants had a PI within the first 36 hours of hospital admission [20]. Differences in prevalence rates in various studies could be related to different settings, populations, and healthcare quality.

Patients with PI on admission had statistically lower BS scores (12.35±2.72 versus 16.53±3.6). Admission BS could be an easy predictive instrument for older adults because of its ability to be an indicator of frailty, the need for a rehabilitation facility and even mortality [21, 22]. Despite these benefits of BS, previous studies reported particular limitations in its ability to predict PI due to missing parameters in its evaluation [23]. For example, BS appeared to underestimate the impact of incontinence on PI occurrence [24]. Accordingly, we studied the potential significance of particular clinical features such as incontinence and selected biochemical parameters such as CAR. CAR was a novel inflammatory index in various diseases [11]. The study demonstrated significantly higher values among those having PI, supporting its potential role in PI occurrence. It could be related to the increased serum CRP and lower serum albumin levels in those with PI. It coincides with previous studies reporting that increased CRP is associated with decreasing mobility and subsequent higher risk of PI [10, 25]. Also, the lower serum albumin and TPs could be related to malnutrition, a common problem among hospitalized and community-dwelling older patients, making it a well-known risk factor of PI [26].

Based on Pearson's correlation analysis, the study showed a significant positive linear correlation between the BS and serum albumin (r 0.31, p-value <0.001), coinciding with a previous study reporting a positive but stronger correlation (r 0.55) [26]. Notably, BS had a negative and significant correlation with CCI, CRP, and CAR. Our findings mean that higher values of CCI, CRP, and CAR are associated with a higher risk of PI. A previous study also highlighted the role of multi-morbidity and reported it as a risk factor for PI [27]. These findings are similar to previous results showing a negative correlation between BS and CRP (r -0.15, p-value 0.295) [26], as elevated CRP correlates with inflammation and poor general medical condition and could be used as a laboratory biomarker in PI [28]. Accordingly, the provision of novel predictive models containing these laboratory biomarkers could overcome reported limitations of BS in PI prediction in some studies [23, 29]. Regarding CBC parameters, the study did not show a significant difference regarding haemoglobin level, contrary to its reported significance in other studies [9, 29]. The role of haemoglobin seems controversial to some extent. Pieper et al. performed a prospective observational study on 694 patients and used a two-sample t-test to compare patients with and without PI that showed significantly lower haemoglobin among those with PI [27]. Anaemia could be related to acute phase reaction, inflammation, and malnutrition with subsequent poor oxygen supply to tissues, poor wound healing, and the occurrence of PI [28]. But other studies reported that high haemoglobin level was associated with PI in patients with respiratory disorders as a compensatory mechanism for chronic respiratory failure [28]. Also, the study revealed that high TLC was associated with PI, coinciding with previous studies that showed leucocytosis as a poor prognostic marker of PI and attributed it to high neutrophils count due to inflammation triggered by skin injury [27, 30].

Regarding demographic data, conflicting data were reported in a previous narrative synthesis involving heterogeneous studies [9]. This study did not show a significant difference regarding age compared to the reported association between older age and PI in other studies [9, 27, 29]. Also, the study did not show a significant difference regarding gender that coincides with reports of the global burden of PI [2]. But it contradicts the reported higher prevalence of PI among males in other studies [9, 31]. Assessing the significance of both age and gender needs further evaluation as the current study lacks stratifying patients by age, gender, and socio-demographic index resulting in an inability to determine the age-standardized incidence and prevalence rates [2].

The current study showed that those having multi-morbidity as evidenced by CCI were significantly associated with the presence of PI at the time of hospital admission, coinciding with other studies [20]. Particular diseases and geriatric syndromes such as dementia, urinary/faecal incontinence, DM, CKD, and old stroke/TIA were significantly associated with the presence of PI on admission. Dementia is a consistent risk factor for PI among older patients, as several studies supported the role of dementia-related mobility problems, cognitive deterioration, and functional decline in the pathogenesis of PI [1]. Recent studies showed that patients with advanced dementia have a higher prevalence of PI with other chronic conditions [32]. It could be related to direct and indirect causes such as immobility, infections, medication adverse effects, malnutrition, and increased risk of falls [33]. Also, incontinence was frequently associated with a higher overall prevalence of PI, especially for full-thickness PI, as supported by the 2013-2014 international pressure ulcer prevalence surveys that showed a higher prevalence of PI among incontinent participants (16.3 % versus 4.1%) [34]. Incontinence-associated dermatitis is a good explanation for this well-known association [24, 35].

Regarding other comorbidities, both DM and CKD were significantly associated with PI, as supported by other studies reporting a significant association between both DM and CKD with PI with an odds ratio of 5.58 (95% CI: 1.83-18.70) and 1.75 (95% CI: 1.27-2.39), respectively [29, 36]. Also, old cerebrovascular stroke/TIA was significantly associated with PI, as supported by several studies [33]. It could be related to immobilization, medication side effects, increased risk of falls, post stoke pneumonia and hospitalization [33]. In a study including community-dwelling stroke patients in Thailand, the prevalence of PI was very high and was associated with moisture, friction, and malnutrition [37]. Chronic respiratory

diseases were not associated with PI among the studied sample of patients, compared to a previous study reporting that 810 (35.0%) of 2313 patients with hospital-acquired PI suffered from chronic respiratory disorders [38]. This association could be related to tissue hypoxia, poor mobility, corticosteroid intake, and sarcopenia [33].

Strengths and Restrictions of the Study

To the best of our knowledge, it is the first study investigating the utility of CAR in PI with the provision of a cut-off for diagnosis. It also provides valuable information regarding the association between PI and common geriatric syndromes such as dementia and incontinence. The main restrictions are the inclusion of a relatively small sample size in a single hospital and the absence of staging of PI to determine the association between various risk factors with separate stages of PI. Also, the study lacks stratification of patients based on age, sex, and sociodemographic index with possible confounding effects on the results. Further longitudinal multicentre studies are appreciated to ascertain the potential value of novel inflammatory mediators in PI risk and provide new effective models or tools to mitigate PI among hospitalized geriatric patients.

CONCLUSION

Particular attention to PI is essential from the first few hours of hospitalization of geriatric patients. Early understanding of the patient's risk situation derived from various clinical features and laboratory biomarkers is clinically beneficial as healthcare providers can take effectual strategies to mitigate PI occurrence or progression at the hospital. The findings show a profile for the high-risk patients as those with particular clinical features such as multi-morbidity, dementia, and incontinence and those with specified biochemical markers such as lower serum albumin and higher TLC and CAR. The results also support the potential role of CAR as a novel biomarker in PI among geriatric patients, which is unique to this study and needs further assessment in future multicenter longitudinal studies.

Author contributions: **Elsorady:** design/conceptualization, participants' selection, data collection/entry, and manuscript drafting. **Elsorady & Nouh:** data analysis, data interpretation, and manuscript revision. All authors have agreed with the results and conclusions.

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Ethics declaration: The protocol was revised and approved by Geriatrics and Gerontology Department Members and the Ethical Committee of the Faculty of Medicine at Ain Shams University (Ethical approval code: FMASU R 58/2022).

Declaration of interest: No conflict of interest is declared by authors.

Data sharing statement: Data supporting the findings and conclusions are available upon request from the corresponding author.

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