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Original Article

Predictors of Multi-Drug Resistant Gram-Negative Bacterial Infection in Critically Ill Older Adults

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ABSTRACT

Background/Purpose: Multi-drug resistant Gram-negative bacterial (MDR-GNB) infection has a higher risk of morbidity and mortality. The study aims to identify the incidence and predictors of MDR-GNB infection in critically ill older adults.

Methods: A prospective cohort study including 297 critically ill older adults. These patients were newly admitted to high dependency units (HDUs) in a tertiary care Geriatrics hospital, from April 1, 2019, to January 4, 2020. Collection of demographic, clinical, and laboratory data on index hospitalization was done through reviewing participant's medical records and direct questioning for each patient/proxy about potential risk factors. Followed by observation of the emergence of MDR-GNB infection during the HDUs stay.

Results: Incidence of MDR-GNB infection was 41.1%. Univariate analysis showed variables significantly associated with MDR-GNB infection including Neutrophil-lymphocyte ratio, Lymphocytes% and Monocytes% on admission, presence of diabetes mellitus (DM), chronic respiratory disease and dementia in clinical history, recent hospitalizations within the last 3 months, length of stay (LOS) in recent hospitalizations and presence of pressure ulcers/wounds before admission. Multivariate analysis showed that dementia in clinical history and monocytes % on admission were independent predictors with an odds ratio of 3.86 (P =0.003, 95% CI: 1.60-9.31) and 1.16 (P =0.012, 95% CI: 1.03-1.31) respectively. A predictive nomogram was constructed with an area under the curve .70 (P =0.000, 95% CI: 0.60-0.79).

Conclusion: The incidence of MDR-GNB infection in critically ill older adults was 41.1%. Dementia in clinical history and monocytes % on admission were predictors for MDR-GNB infection. A novel nomogram was formulated.

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1. INTRODUCTION

Antibiotic resistance is a major public health problem resulting in limitation in the available treatment options in clinical settings.[1] According to the World Health Organization, multi-drug resistant Gram-negative bacterial (MDR-GNB) infection has a priority due to the higher risk of morbidity and

mortality with an urgent need for newer antibiotics.[2] Geriatric patients are more prone to the suboptimal treatment of infections and inappropriate antibiotics use because of the difficulty in obtaining diagnostic specimens and a timely diagnosis. Also, residents in skilled nursing facilities (SNFs) are more vulnerable to infections and acquisition of multi-drug resistant (MDR) pathogens because of multimorbidity, cognitive impairment, functional limitations, inappropriate antimicrobials use and higher illness severity.[3] MDR-GNB colonization represents a special concern among patients with advanced dementia in nursing homes.[4] Older patients may act as vectors, transmitting pathogens to hospitals during transitions.[3] These facts highlight the importance of predicting MDR-GNB infection in older adults in acute care settings.

Several studies reported various predictors of infection with MDR pathogens among critically ill patients including previous hospitalization, use of antibiotics,[5,6] older age and residence in a long-term care facility (LTCF).[7] Recently a combination of various risk factors in a predictive nomogram has been proposed for convenient use in intensive care units (ICUs).[8] Unfortunately, there is no available nomograms, specified for the prediction of MDR-GNB infection in critically ill Geriatric patients. This study aims to identify the incidence and predictors of MDR-GNB infection in critically ill older adults with formulation of an age-specific, predictive nomogram.

2. METHODS

2.1. Study Design, Setting and Participants

A prospective observational study conducted at Geriatrics hospital, a tertiary care University hospital for acute management of older adults (60 years old and above). The study included patients who were newly admitted at HDUs (Intensive care unit/ Intermediate care unit) from April 1, 2019, to January 4, 2020. Patients, who were admitted more than one time till the end of January 2020, were included without duplication, utilizing their clinical and laboratory data of the first/index admission. Follow up of each patient was extended throughout the stay at HDUs till either discharge alive or death. The primary outcome was the occurrence of MDR-GNB infection at HDUs. Exclusion criteria include patients who had documented MDR-GNB infection before admission, patients who had missing first/index admission data, those who were missed during the observational period, and those who were discharged against medical advice and transferred to another hospital during treatment.

2.2. Demographic, Clinical and Laboratory Data

Demographic, clinical and laboratory data collection was performed through 2 steps: the first one was a review of patient's medical records for age, gender, comorbidities, vital data on admission, use of mechanical ventilation on the first day of admission and use of intravenous vasopressors/inotropic support on the first day of admission. The second step was direct questioning for each patient/proxy about recent hospitalizations within the last 3 months, length of stay (LOS) at hospitals over the last 3 months, residence at LTCF, use of intravenous fluids at home, history of mechanical ventilation and/or hemodialysis, and presence of chronic wounds or pressure ulcers before admission. It was followed by observation of the emergence of MDR-GNB infection during the HDUs stay.

Laboratory data on admission includes a complete blood picture, the levels of albumin, creatinine, total bilirubin, alanine aminotransferase, C-reactive protein (CRP) and oxygenation index (PaO2/FiO2). Blood samples were assessed at the clinical laboratories of Ain Shams University hospitals. Different clinical specimens including urine, sputum, bronchoalveolar lavage, blood, central venous catheter, and wound swabs were collected by nursing staff. Urine specimens were collected midstream through a urinary catheter. Blood cultures were incubated in Oxoid bottles. Sensitivity to antibiotics was done by disc diffusion method. Extended-Spectrum Beta-Lactamase (ESBL)-producing pathogens identified by the Double Disc Synergy Test and Carbapenemases producing bacteria identified as per Clinical Laboratory Standards Institute guidelines.[9]

2.3. Variables of Interest and Measurements

In contrary to colonization with MDR-GNB, an episode of infection with MDR-GNB was identified by the presence of compatible symptoms and signs with MDR-GNB isolates in clinical specimens and supported by radiology, and/or serology. In the case of polymicrobial infection, MDR-GNB infection was considered positive in the presence of MDR-GNB isolates in any clinical specimen of a patient. Accordingly, patients were categorized into those with and without MDR-GNB infection. Multi-drug resistance was defined as resistance to one or more agent in 3 or more categories of antibiotics.[10] Gram-negative bacteria included Klebsiella pneumoniae, Acinetobacter species, Escherichia coli, Pseudomonas aeruginosa, Proteus species and ESBLs producing pathogens. ESBLs producing pathogens were defined by the production of β-lactamases that induces hydrolysis of penicillins; aztreonam; and first-, second- and third-generation cephalosporins leading to resistance to these antibiotics but not carbapenems.[11] Predicting the occurrence of infection with MDR pathogen was performed by utilizing a nomogram including scores of 3 risk factors: gender, CRP and Pitt score on admission to identify total nomogram points and probability.[8] The immunosuppressive status

referred to having any of the following: acquired immune deficiency syndrome, active malignancy, End-stage renal disease (ESRD), splenectomy, and long-term immunosuppressant use.

Based on laboratory data on admission, the Neutrophil-lymphocyte ratio (NLR) was calculated by dividing the relative neutrophils to lymphocytes count.[12] PaO2/FiO2 ratio (PFR) was calculated by dividing PaO2/FiO2 to assess initial oxygenation.[13] Estimation of PFR from oximeters is used for patients who had normal oxygen saturation on admission without available PaO2 in arterial blood gases parameters.[14]

Based on clinical data on admission, acute illness severity assessed by simplified acute physiology score II (SAPS II),[15] and Pitt bacteremia score.[16] Pitt bacteremia score included assessment of mental status, the presence or absence of fever, hypotension, mechanical ventilation and cardiac status.[16]

2.4. Statistical Analysis

Values were presented as means±*SD* or as numbers and proportions, as appropriate. The relations between qualitative variables were evaluated by Chi-square test or Fisher's exact test, as indicated. Continuous variables were checked for normality by using Shapiro-Wilk test. As data were normally distributed, unpaired t-test was used. Variables with *P* values ≤0.1 in univariate analysis were introduced in a forward stepwise logistic regression model to detect independent predictors of MDR-GNB infection. ROC curve was used to assess the sensitivity, specificity and area under the curve of the newly developed model. All tests were bilateral and a *P* value of 5% was the limit of statistical significance. The analysis was performed by statistical package software IBM-SPSS version 21 and StataMP 13.

2.5. Ethical Consideration

The study protocol was revised and approved by Geriatrics hospital ethics review board and Research Ethics Committee of the faculty of Medicine at Ain Shams University (Code: FMASU R 18/ 2020).

3. RESULTS

The screening of eligible patients for enrolment in the study is presented in a flow chart (Supplementary figure.1). Total study participants in the final statistical analysis were 297 critically ill older adults, including 102 male (34.3%) and 195 female patients (65.7%). The mean age of participants was 73.9±8.8 years. The most common cause of admission was respiratory infection/insufficiency in 64 patients (21.5%) followed by sepsis in 41 patients (13.8%).

Participant's characteristics including quantitative and qualitative risk factors for MDR-GNB infection are described in (Tables 1, 2 and Supplementary Tables S1, 2). There were a total of 122 patients (41.1%) who had MDR-GNB infection. Regarding the distribution and frequency of MDR-GNB infections among participants, the most common site of infection was the respiratory tract (37%) and the most common culprit microorganism was Klebsiella pneumoniae (32%) as described in Figure 1. A, B.

Logistic regression analysis was conducted to measure the association between each potential risk factor and MDR-GNB infection (Table 3, Supplementary Tables S3 and S4).

Upon univariate analysis, there were no significant differences in the mean age, illness severity scores and basic biochemical parameters reflecting organ function including creatinine, albumin, alanine aminotransferase, total bilirubin and oxygenation index (PFR) between those with and without MDR-GNB infection. There were significant differences between those with and without MDR-GNB infection regarding quantitative risk factors including lymphocytes%, NLR, monocytes% on admission and LOS in recent hospitalizations with a *p*-value of 0.090, 0.011, 0.009, and 0.031, respectively. There were also significant differences between those with and without MDR-GNB infection regarding qualitative risk factors including; the presence of diabetes mellitus (DM), chronic respiratory disease and dementia in clinical history, recent hospitalizations within the last 3 months and the presence of pressure ulcers/wounds before admission with a *p*-value of 0.000, 0.071, 0.010, 0.042, and 0.007, respectively.

After multivariate analysis, the presence of dementia in clinical history and monocytes% on admission were found to be independent predictors for MDR-GNB infection. This result shows that having dementia would increase the odds of having a MDR-GNB infection by 3.87 times. Also, with each 1% increase in monocytes, the odds of MDR-GNB infection would increase by 0.17 times. The 95 CI means that by 95% we are confident that having dementia would increase the odds of MDR-GNB infection from 0.61 to 9.31 times. While, a one percent increase in monocytes would increase the MDR- GNB infection odds from 0.03 to 0.32 times.

The two independent predictors were combined in a novel predictive nomogram (Figure 2. A, B). This nomogram was able to explain 18.7% of the variability of MDR-GNB infection as indicated by Nagelkerke R Square value and was able to correctly predict MDR-GNB infection by 69.3%. At a cutoff value of 0.34, this nomogram has a sensitivity of 71.4% and a specificity of 68.2% with an area under the curve of 0.70 (*P* = 0.000, 95% CI: 0.60-0.79) (Figure 3).

Table 1. Participant's characteristics and quantitative risk factors for MDR-GNB infection in critically ill older adults

Quantitative risk factors	Means±*SD* All (n)	MDR-GNB infection	NO MDR-GNB infection	*P*
Age	73.9±8.8 (297)	74.5±8.7 (122)	73.5±8.9 (175)	0.312
TLC (x 10^3/μL)	12.1±8.8 (297)	11.5±5.5 (122)	12.6±10.5 (175)	0.271
Neutrophil%	75.4±16.1 (134)	72.4±16.5 (44)	76.8±15.8 (90)	0.138
Lymphocyte%	13.8±11.1 (133)	16.2±11.1 (43)	12.7±11.0 (90)	0.090
NLR	11.7±15.5 (133)	7.9±6.8 (43)	13.5±17.9 (90)	0.011
Monocytes%	6.6±3.7 (130)	7.8±3.8 (42)	6.0±3.6 (88)	0.009
Eosinophils%	1.3±2.1 (129)	1.3±2.3 (42)	1.3±2.0 (87)	0.865
Basophils%	0.6±0.9 (128)	0.5±0.4 (42)	0.7±1.0 (86)	0.481
Hemoglobin (g/dL),	10.5±2.2 (296)	10.4±2.2 (121)	10.6±2.3 (175)	0.440
Platelets (x 10^3/μL)	236.2±114.1 (296)	242.9±116.4 (121)	231.6±112.7 (175)	0.406
Creatinine (mg/dL)	1.8±1.7 (295)	1.8±1.9 (122)	1.8±1.5 (173)	0.719
CRP (mg/L)	99.3±91.2 (267)	99.3±86.1 (114)	99.3±95.2 (153)	0.999
Albumin (g/dL)	2.7±0.6 (274)	2.6±0.6 (117)	2.7±0.6 (157)	0.205
Total bilirubin (mg/dL)	1.1±1.7 (261)	1.0±1.7 (110)	1.2±1.6 (151)	0.362
ALT (IU/L)	31.7±78.3 (267)	32.0±68.3 (113)	31.4±85.1 (154)	0.948
PFR	342.6±131.4(277)	332.4±128.5(118)	350.2±133.3 (159)	0.268
GCS	12.4±3.1 (291)	12.1±3.1 (119)	12.5±3.1 (172)	0.305
RBS (mg/dL)	177.4±93.4 (289)	181.4±84.4 (118)	174.7±99.4 (171)	0.548
Recent hospitalizations LOS (days)	9.5±14.5 (257)	11.8±16.5 (111)	7.8±12.7 (146)	0.031
SAPS II points	37.0±10.2 (233)	37.1±8.9 (98)	36.9±11.0 (135)	0.887
Pitt score points	15.5±8.8 (282)	16.1±8.6 (112)	15.2±8.9 (170)	0.429
Predictive nomogram probability	0.4±0.1 (254)	0.5±0.1 (105)	0.4±0.1 (149)	0.302

Abbreviations: NLR, Neutrophil-lymphocyte ratio; PFR, PaO2/FiO2 ratio; RBS, Random blood sugar; SAPS II, simplified acute physiology score II; TLC, Total leucocyte count; CRP, C-reactive protein; ALT, Alanine aminotransferase; GCS, Glasgow coma scale; LOS, length of stay.
Normal range of TLC (4-10 x 10^3/μL), Hemoglobin (12-15g/dL), Platelets (150-410 x 10^3/μL), Creatinine (0.6-1.2mg/dL), CRP (<6mg/L), ALB (3.5-5.7g/dL), Total bilirubin (0.3-1mg/dL), ALT (7-52IU/L), RBS (80-140mg/dL).

Table 2. Participant's characteristics and qualitative risk factors for MDR-GNB infection in critically ill older adults

Qualitative risk factors	Number (%)	MDR-GNB infection	NO MDR-GNB infection	*P*
Male: female	102 (34.3):195 (65.7)	43 (42.2):79 (40.5)	59 (57.8):116 (59.5)	0.784
Cause of admission				0.411
Respiratory infection/insufficiency	64 (21.5)	27 (42.2)	37 (57.8)	
Sepsis	41 (13.8)	22 (53.7)	19 (46.3)	
Circulatory Collapse	23 (7.7)	6 (26.1)	17 (73.9)	
CVA	38 (12.8)	14 (36.8)	24 (63.2)	
Immunosuppressive state	55 (18.5)	19 (34.5)	36 (65.5)	0.275
Recent hospitalizations	194 (68.8)	89 (45.9)	105 (54.1)	0.042
IV fluids infusion at home	72 (26.8)	28 (38.9)	44 (61.1)	0.484
LTCF residence	8 (3.0)	4 (50.0)	4 (50.0)	0.724
Previous mechanical ventilation.	21 (7.6)	11 (52.4)	10 (47.6)	0.307
Previous hemodialysis	17 (6.3)	9 (52.9)	8 (47.1)	0.322
Presence of pressure ulcer/wounds before admission	112 (39.9)	58 (51.8)	54 (48.2)	0.007
Comorbidities				
CVD	229 (77.1)	96 (41.9)	133 (58.1)	0.587
DM	140 (47.1)	73 (52.1)	67 (47.9)	0.000
Old CVA/TIA	98 (33.0)	42 (42.9)	56 (57.1)	0.662
CKD/ESRD	71 (23.9)	33 (46.5)	38 (53.5)	0.289
Chronic liver disease	63 (21.2)	24 (38.1)	39 (61.9)	0.588
Malignancy	46 (15.5)	17 (37.0)	29 (63.0)	0.537
Chronic respiratory disease	45 (15.2)	13 (28.9)	32 (71.1)	0.071
History of Dementia	99 (33.3)	51 (51.5)	48 (48.5)	0.010

Abbreviations: CVD, Cardiovascular disease; DM, Diabetes mellitus; CVA/TIA, Cerebrovascular accidents/Transient ischemic attacks; CKD/ESRD, Chronic kidney disease/End-Stage Renal disease; LTCF, Long term care facility.

Table 3. Logistic regression analysis of predictive factors for MDR-GNB infection in critically ill older adults

Predictive factors	Univariate analysis		Multivariate analysis	
	OR (95%-CI)	*P*-value	OR (95%-CI)	*P*-value
NLR	0.957 (0.915-1.002)	0.061	-	-
Monocytes %	1.139 (1.029-1.260)	0.012	1.166 (1.034-1.316)	0.012
Recent hospitalizations LOS (days)	1.019 (1.001- 1.037)	0.037	-	-
Recent hospitalizations	1.724 (1.018- 2.920)	0.043	-	-
Presence of pressure ulcer/ wounds before admission	1.951 (1.200- 3.174)	0.007	-	-
Comorbidities				
DM	2.401 (1.496- 3.855)	0.000	-	-
Chronic respiratory disease	0.533 (0.267-1.064)	0.074	-	-
History of Dementia	1.901 (1.165- 3.101)	0.010	3.869 (1.607- 9.310)	0.003

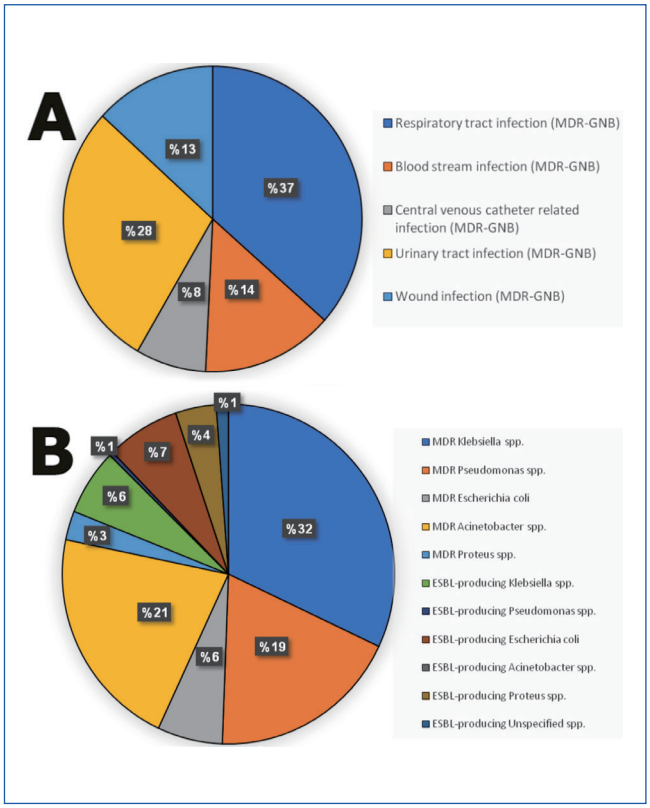
Abbreviations: OR, Odds ratio; NLR, Neutrophil-lymphocyte ratio; DM, Diabetes mellitus; LOS, length of stay.

4. DISCUSSION

Although risk factors for infection with MDR pathogens in hospitalized adults are frequently studied, data for MDR-GNB infections in critically ill Geriatric patients are scarce. This prospective cohort study aimed to identify the incidence and predictors of infections caused by MDR-GNB in critically ill older patients. The present study revealed 2 important findings; First, the incidence and distribution of MDR-GNB infection among older adults in HDUs at a tertiary care University hospital, specialized for care of older adults (aged ≥60 years old). Second, was the provision of an age-specific predictive nomogram for MDR-GNB infection in this vulnerable group of patients.

The present study shows important information about the distribution and frequency of different MDR-GNB species. MDR-GNB infections occurred in 122 patients (41.1%) as supported by microbiology with radiology, and/or serology, confirming the high incidence of this infection in critically ill older patients. This finding coincides with the results of other studies.[17-18] Gram-negative bacteria have special importance as Escherichia coli, Enterobacter species, Klebsiella pneumoniae, Acinetobacter baumannii, Pseudomonas aeruginosa are associated with a high risk of resistance to multiple antibiotics.[17] Various studies showed different frequencies of multidrug-resistance rate for different microorganisms. In the present study, Klebsiella pneumoniae was the most frequent MDR-GNB at HDUs (32% of MDR-GNB infections in the studied cohort), supporting the reported high rate of infection with carbapenamase-producing Klebsiella pneumoniae in another prospective multinational study involving hospitals in 36 countries.[19] But it is different from the results of another single centre study demonstrating Acinetobacter baumannii as the most frequent MDR

Figure 1. A, B. Frequency and distribution of MDR-GNB infections in critically ill older adults
(A) Sites of MDR-GNB infections in critically ill older adults
(B) Species of MDR-GNB infections in critically ill older adults



microorganism in ICUs.[8] These different results support the variability in frequency and distribution of MDR pathogens, based on participant's characteristics and clinical settings. The present study also reflects the increasing frequency of ESBL producing Gram-negative bacteria in critically ill older patients (19% of MDR-GNB infections in the studied cohort). It supports previous reports on the ongoing trends of MDR-GNB infection and the increasing infection rate with ESBL producing Gram-negative bacteria in

Figure 2. A, B. A Novel Predictive Nomogram. The nomogram predicts the emergence of MDR-GNB infection in critically ill older patients. To use the nomogram: First, determine monocytes% on admission and the presence or absence of dementia then draw a line straight down to establish the score for each covariate separately. Second, add the scores for each covariate together, and locate the total score then draw a line straight up to the linear axis to obtain the probability ranging from 20 to 80%

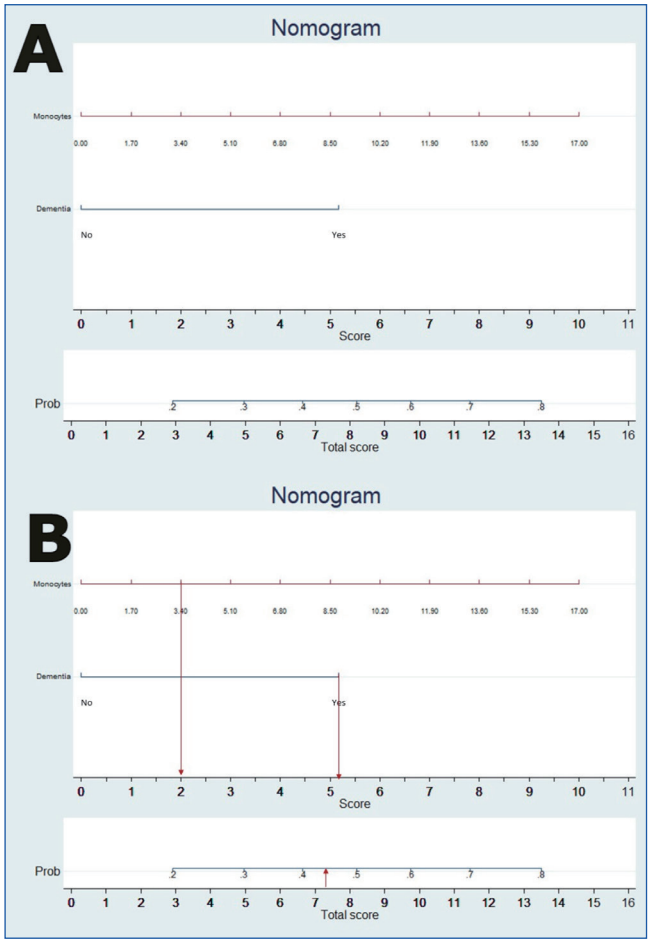
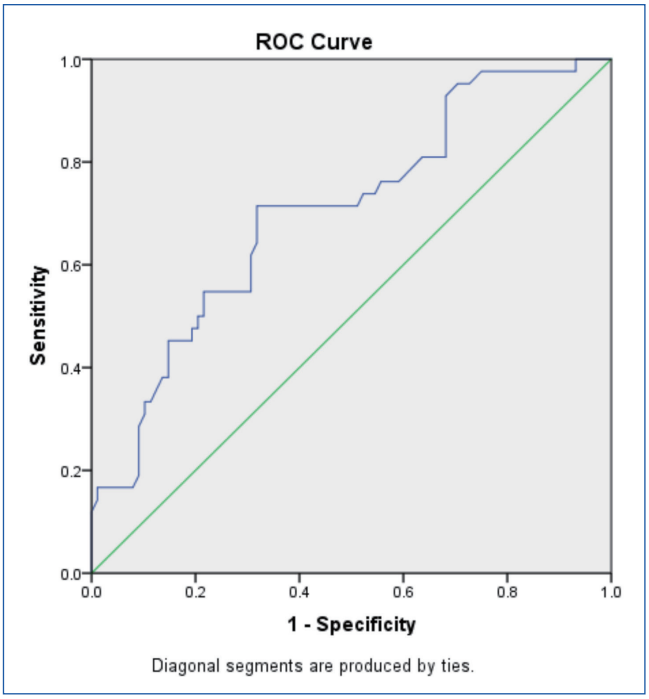


Figure 3. Receiver Operating Characteristic (ROC) curve of the Novel Predictive Nomogram: Area Under the Curve (AUC) of the Novel Predictive Nomogram is 0.70 (P = 0.000, 95% CI: 0.60-0.79)



ICUs in Europe and the United States from 2009 to 2011.[20] According to the Antibiotic Resistance Threats report in 2019, Carbapenem-resistant Acinetobacter and Carbapenem-resistant Enterobacteriaceae are considered urgent threats requiring aggressive and urgent action. While ESBL-producing Enterobacteriaceae and MDR Pseudomonas aeruginosa are considered serious threats.[1]

On the other hand and besides the discovered predictive role of both dementia in the clinical history and monocytes % on admission at HDUs, Patients with MDR-GNB infection had lower NLR on admission. This finding correlates with the results of another retrospective study, demonstrating that lower NLR could predict MDR Pseudomonas aeruginosa infection in patients with hospital-acquired pneumonia.[21] Also, the study showed that certain clinical indicators such as the presence of pressure ulcers/wounds before admission, recent hospitalizations within the last 3 months and LOS in recent hospitalizations had a significant association with MDR-GNB infection, coinciding with the finding of previous studies.[22-24] Also the presence of DM and chronic respiratory disease in clinical history had a significant association with in-hospital emergence of MDR-GNB infection, supporting the reported role of these comorbidities as risk factors for this infection in the previous studies.[25,26]

After multivariate regression analysis, this study showed independent predictors of MDR-GNB infection during critical illness. Dementia in the clinical history was the only comorbidity that remained as an independent predictor for MDR-GNB infection with an odds ratio of 3.86 (*P* =0.003, 95% CI: 1.60-9.31). This finding supports the reportedly high rates of colonization with MDR-GNB in patients with dementia and the extensive use of antimicrobials in these patients.[27] This finding also coincides with the importance of dementia as a risk factor for the occurrence of MDR bacterial infection in LTCF.[22] Dementia was also more important than the overall acute illness severity scores including SAPS II and Pitt bacteremia score on admission. Neither SAPS II nor Pitt bacteremia score was significantly associated with MDR-GNB infection. Similarly, other studies demonstrated that acute illness severity scores can not necessarily predict MDR bacterial infection during critical illness.[28]

On the other side, monocytes % on admission at HDUs was the second significant predictor for MDR-GNB infection in participants, with an odds ratio of 1.16 (*P* =0.012, 95% CI: 1.03-1.31). This finding highlights the importance of differential blood count

in predicting this infection during critical illness. As with each 1% increase in monocytes, the odds of MDR-GNB infection would increase by 0.17 times. It could be explained by the well-known fact about monocytes recruitment from bone marrow to bloodstream and migration into tissues during inflammation, degenerative diseases and infections.[29] This finding needs further studying in other prospective multicenter studies.

The present study did not show a significant association between MDR-GNB infection with chronologic age, history of cerebrovascular accidents and residence in LTCF as reported in other studies.[30] Despite the high prevalence of MDR-GNB colonization and infection in residents of LTCF.[22] The study cannot demonstrate the significance of the residence in LTCF as a risk factor for MDR-GNB infection that could be attributed to the relatively small number (8 patients) of LTCF residents in the study.

Regarding immunosuppression as a risk factor for MDR-GNB infection. There is heterogeneity in defining the immunosuppressive state between various studies. In the present study, immunosuppression was defined as the presence of any of the following conditions; acquired immune deficiency syndrome, active solid organ or haematological malignancy, ESRD, splenectomy, and long-term immunosuppressant use. There was no significant association between the presence of immunosuppression and MDR-GNB infection. Similar to other studies demonstrating that immunosuppression is not independently associated with the occurrence of MDR bacterial infection during critical illness.[8] These findings are contradicting the reported importance of immunosuppression as a risk factor for MDR-GNB in LTCFs.[22]

Finally, the present study did not support the use of the predictive nomogram of Wang et al.[8] in critically ill older adults as neither the total nomogram points/ probability nor any one of its components including CRP, gender and Pitt score were significantly associated with the occurrence of MDR-GNB infection among participants.

Limitations and Strengths:

The study has some limitations: it is a single-center study including a relatively small sample size especially for differential blood count related variables. Second, the diagnosis of dementia was based on clinical history from the patient's proxies without using cognitive assessment tools. Third, despite the reported significance of previous exposure to antibiotics as a risk factor for bacterial infection with MDR pathogens in various studies,[30] it can't be accurately assessed in the current study due to poor recall and reluctant documentation of previous treatment regimes for patients.

Strengths of the study are its prospective design with the inclusion of critically ill Geriatric patients and investigating important risk factors, some of them are first to be assessed among these vulnerable patients such as the predictive nomogram of Wang et al.,[8] Pitt score and NLR. Also, it is the first study demonstrating the predictive role of dementia besides monocytes % for MDR-GNB infection in critical care settings with the provision of an age-specific, predictive nomogram.

5. CONCLUSION

The present study confirms the increasing incidence of antibiotic resistance among older adults at hospitals. It highlights the global challenge in the treatment of carbapenem-resistant Gram-negative bacteria and ESBL producing Enterobacteriaceae that forces health care providers to use different antibiotics such as colistin and intravenous carbapenems with subsequent increase in toxicity and cost. These data necessitate immediate actions such as antibiotic stewardship and strict infection control measures. The study provides a novel predictive nomogram for MDR-GNB infection in critically ill Geriatric patients. This nomogram needs external validation and further studying in other prospective multicenter studies.

CONFLICTS OF INTEREST

The author declares no conflict of interest.

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None

Supplementary data

https://drive.google.com/file/d/1XA_nYoI21sLYizv13oZaAuizZxV45Nr8/view?usp=sharing

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