

Empirical Antibiotics' Impact on Hospital Stay and Mortality in Community-Acquired Pneumonia

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ABSTRACT

Introduction: Community-acquired pneumonia (CAP) shows a high prevalence rate in adult patients. Bacterial infections are the most common etiology of CAP cases and can lead to patient hospitalization, morbidity, and mortality. Empirical antibiotics can be given to CAP patients to prevent worsening. This study aims to analyze the appropriateness of empirical antibiotics, according to guidelines on length of stay and mortality, in CAP patients.

Methods: This observational retrospective study used medical record data from CAP patients at Sultan Agung Islamic Hospital, Semarang, from January 2023 to December 2024. We evaluated the impact of prescribed antibiotics, based on the 2019 ATS/IDSA guidelines, on length of stay and in-hospital mortality. Data were tested using the Fisher test with a 95% confidence interval (CI).

Result: Significant differences were shown in the type of treatment room and comorbid diseases such as lung disorders, related to patient outcomes (recovery or death). The administration of empirical antibiotics to patients with CAP, as recommended by guidelines on length of hospitalization and patient mortality, demonstrated p-values of 0.683 and 0.166, respectively ($p > 0.05$). The suitability of empirical antibiotics to the guideline did not affect the length of treatment and outcome of CAP patients.

Conclusion: The administration of empirical therapy in accordance with guidelines did not demonstrate a correlation with reduced duration of hospitalisation or decreased mortality. Nevertheless, a significant association was identified between ICU admission, comorbid lung disease, and patient outcomes.

Keywords: Community-acquired pneumonia; empirical antibiotics; length of stay; mortality



GREEN MEDICAL
JOURNAL
E-ISSN 2686-6668

Article history:

Received: 1 September 2025

Accepted: 19 December 2025

Published: 31 December 2025

Published by:

Faculty of Medicine
Universitas Muslim Indonesia

Address:

Jl. Urip Sumoharjo Km. 5, Makassar
South Sulawesi, Indonesia

Email: greenmedicaljournal@umi.ac.id

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Introduction

Pneumonia is an acute infection of the lung parenchyma, which can cause health problems.^{1,2} Community-acquired pneumonia (CAP) is an infection of the lung parenchyma acquired out of the health care environment. Age, smoking, malnutrition, environmental exposures, previous CAP infection, chronic bronchitis/COPD, asthma, impaired respiratory function, poor dental health, use of immunosuppressant therapy, oral corticosteroids, and drugs that decrease gastric acid production may increase the risk of CAP.^{3,4} CAP is a pneumonia with a high prevalence in adult patients. Data shows that more than 1.5 million adult CAP patients require hospitalization each year. CAP is the most common infectious disease causing death.^{5,6} Pneumonia occupies the top 10 hospital inpatient diseases in Indonesia. The crude death rate (CDR) due to pneumonia is 7.6%, the highest when compared to other infectious diseases. The risk of death from pneumonia increases in patients aged >65 years, male gender, and patients with comorbidities.⁷

Most CAP cases are bacterial in origin and contribute substantially to hospitalization burden and mortality. The most common bacteria causing pneumonia include *Streptococcus pneumoniae* (33-50%), *Haemophilus influenzae* (7-16%), *Staphylococcus aureus*, and Enterobacteriaceae including Klebsiella (4-10%). Pseudomonas (0.8-4.5%) and Moraxella (1.2-3.5%) cause less cases of pneumonia. Atypical bacteria can also cause pneumonia including Mycoplasma (4-11%), Legionella (3-8%), Chlamydia (2-7%), and Coxiella (<2%).^{8,9} Antibiotic administration is the main pharmacological therapy in cases of pneumonia caused by bacterial infection. Antibiotic administration is based on the results of bacterial identification and antibiotic sensitivity tests. However, empirical antibiotics can be given in CAP cases because they often cause worsening.^{2,7}

Empiric antibiotics for CAP are recommended before the causative pathogen is known. Empirical antibiotics are given as soon as the diagnosis is made.¹⁰ Empirical antibiotic administration can reduce antimicrobial resistance, reduce treatment costs and the incidence of side effects.^{11,12} Empirical antibiotics according to ATS/IDSA (American Thoracic Society and Infectious Diseases Society of America) are based on selective antibiotics that are effective against the main bacteria that cause CAP.⁶ Antibiotic use in hospitals or clinics is often not in line with established guidelines. Some of the causes of antibiotic use inappropriateness are doctors' habits in prescribing antibiotics, limited availability of certain antibiotics, and replacement of antibiotics due to delegation of responsibility of the doctor in charge. This will affect the prognosis of CAP patients.¹² This study aims to analyse the effect of empirical antibiotic administration on length of stay and mortality in CAP patients in the hospital.

Methods

This study is a retrospective study using medical record data at Sultan Agung Islamic Hospital Semarang from January 2023-December 2024. It received ethical approval from the Bioethics Commission of Sultan Agung Islamic Hospital, Semarang, Indonesia (Approval No. 8/KEPK-RSISA/I/2025). The samples in this study were CAP patients who met the inclusion and exclusion criteria. Patients aged >18 years with a diagnosis of pneumonia/CAP who received empirical therapy were included in the study. Empirical therapy is antibiotic therapy given before knowing the results of culture and antibiotic sensitivity tests. CAP was confirmed based on the diagnostic criteria: (1) the presence of new infiltrates in the lungs on radiographic examination; (2) at least one of the symptoms of lower respiratory tract infection and physical examination results such as fever >38°C, cough with mucus, dyspnea, tachypnea, leukocyte count >12,000 mm³ or <6,000 mm³, abnormal lung auscultation, and changes in mental status in patients aged >70 years. The severity of CAP using the CURB-65/CRB-65 score: decreased consciousness, blood urea nitrogen (BUN), respiratory frequency, blood pressure, and age >65 years. Patients with a diagnosis of HAP, HCAP, and VAP were excluded.

Data collected included patient age, gender, main symptom, treatment room, CURB-65/CRB-65 score, comorbid diseases, and laboratory results. Data on empirical antibiotic administration and route of administration were recorded. The appropriateness of empirical antibiotics was assessed based on the 2019 ATS/IDSA guidelines. Outcomes assessed were length of hospital stay and patient recovery. Patient recovery was rated as recovered and not recovered. Recovery was categorized as a patient going home or there were signs of clinical improvement. Signs of clinical improvement included temperature ≤37.8°C, heart rate ≤100 beats/min, respiratory rate ≤24 breaths/min, systolic blood pressure ≥90 mmHg, did not require oxygenation, and could take antibiotics orally. Patients who did not recover included patients who died or there was no clinical improvement after administering antibiotics for more than 3 days. Data were analyzed using SPSS and tested using Fisher test with 95% confidence interval (CI).

Result

This study involved 214 medical students, 74.3% of whom were under 20 years old, while 25.7% were aged 20 or older. The Body Mass Index (BMI) of respondents was 46.7% normal, 23.8% obese, and 14% underweight. Most of the respondents have early menarche (54.7%), average menarche (36.9%), and late menarche (8.4%). The respondents reported that 52.8% experienced mild dysmenorrhea and 47.2% experienced severe dysmenorrhea. The respondents also reported that 50.9% have good sleep quality and 49.1% have poor sleep quality. Respondent characteristics are shown in Table 1.

Table 1. Characteristics of CAP patients

Characteristics	Recovery (n = 91 (94,8%))	Death (n = 5 (5,2%))	OR (95% CI)	P value
Age				
<65 years old	55 (94,8%)	3 (5,2%)	1,019 (0,162-6,399)	P = 1,000 ^a
>65 years old	36 (94,7%)	2 (5,3%)		
Gender				
Female	48 (94,1%)	3 (5,9%)	0,744 (0,119-4,667)	P = 1,000 ^a
Male	43 (95,6%)	2 (4,4%)		
Main symptom				
Respiratory symptom	77 (95,1%)	4 (4,9%)	0,704 (0,144-3,453)	P = 0,098 ^b
Altered status mental	1 (50%)	1 (50%)		
Other symptom	13 (100%)	0 (0 %)		
Treatment room				
Non intensive	90 (96,8%)	3 (3,2%)	0,017 (0,001-0,239)	P = 0,006 ^a
Intensive (ICU)	1 (33,3%)	2 (66,7%)		
Comorbid disease				
Cardiovascular	15 (16%)	1 (20%)	0,789 (0,082-7,567)	P = 1,000 ^a
Hypertension	16 (18%)	0 (0 %)	1,067 (1,008-1,129)	P = 0,586 ^a
DM type 2	16 (18%)	2 (40%)	0,320 (0,049-2,074)	P = 0,235 ^a
Electrolyte imbalance	9 (10%)	1 (20%)	0,439 (0,044-4,365)	P = 0,430 ^a
Other pulmonary disease	28 (31%)	4 (80%)	0,111 (0,012-1,040)	P = 0,041 ^a
CKD	8 (9%)	0 (0 %)	1,060 (1,007-1,116)	P = 1,000 ^a
CURB-65/CRB-65 score				
0	30 (96,8%)	1 (3,2%)	1,109 (0,342-3,591)	P = 0,882 ^b
1	43 (93,5%)	3 (6,5%)		
2	16 (94,1%)	1 (5,9%)		
3	2 (100%)	0 (0%)		
Laboratory tests				
Culture	13 (92,9%)	1 (7,1%)	0,663 (0,197-2,228)	P = 0,807 ^b
Gram stain	28 (93,3%)	2 (6,7%)		
Not performed (Culture/Gram stain)	50 (96,2%)	2 (3,8%)		
Route of administration				
Intravena	82 (90%)	5 (100%)	0,943 (0,895-0,993)	P = 1,000 ^a
Per-oral	9 (10%)	0 (0%)		
Length of stay				
1-7 days	85 (93%)	4 (80%)	3,542 (0,340-36,859)	P = 0,321 ^a
8-14 days	6 (7%)	1 (20%)		

^aFisher test; ^bLikelihood ratio

The microbiological tests performed in this study were sputum culture and Gram stain. *Klebsiella pneumoniae* was the most common pathogen isolated from cultures of CAP patients. Table 2. presents the bivariate analysis of the effect of antibiotics according to guidelines on outcomes and length of stay. The results showed no difference in outcomes or length of stay between patients who received empirical antibiotic therapy according to guidelines ($p > 0.05$). Empirical antibiotic groups used in the study are listed in Table 3. Antibiotics given to CAP patients are predominantly in monotherapy rather than combination therapy. Common antibiotics used in this study were intravenous fluoroquinolones, including levofloxacin and moxifloxacin. Antibiotic therapy, depending on the antibiotic type, did not affect the outcome or the length of hospitalization in CAP patients (p -value > 0.05 ; Table 3).

Table 2. Bivariate analysis of empirical antibiotics on length of hospitalization

Variables	Length of stay		P value	Outcome		P value
	1-7 days (n=89 (92,7%))	8-14 days (n=7 (7,3%))		Recovery (n = 91 (94,8%))	Death (n = 5 (5,2%))	
Empirical antibiotics According to the guideline	29 (90,6%)	3 (9,4%)	$P = 0,683^a$	32 (100%)	0 (0%)	$P = 0,166^a$
Not according to the guideline	60 (93,8%)	4 (6,3%)		59 (92,2%)	5 (7,8%)	

^aFisher test

Table 3. Empirical antibiotics of CAP patients in hospital

Types of antibiotics	Recovery (n = 91 (94,8%))	Death (n = 5 (5,2%))	P value	Length of stay		P value
				1-7 days (n = 89 (92,7%))	8-14 days (n = 7 (7,3%))	
3rd generation cefalosporin + <i>beta</i> <i>lactamase inhibitor</i>	28 (90,3%)	3 (9,7%)	$P = 0,344^a$	29 (93,5%)	2 (6,5%)	$P = 0,054^a$
3rd generation cefalosporin	23 (92%)	2 (8%)		25 (100%)	0 (0%)	
Fluoroquinolone	32 (100%)	0 (0 %)		29 (90,6%)	3 (9,4 %)	
Aminoglycoside	4 (100%)	0 (0 %)		3 (75%)	1 (25 %)	
Penicillin + <i>beta</i> <i>lactamase inhibitor</i>	3 (100%)	0 (0 %)		3 (100%)	0 (0 %)	
Penicillin	1 (100%)	0 (0 %)	0 (0%)	1 (100 %)		

^aLikelihood ratio

Discussion

This study aims to assess the effect of empirical antibiotic administration on patient mortality and length of hospital stay. The results show that empirical antibiotic administration in accordance with guidelines is not significantly associated with reduced mortality or shorter hospital stays. These findings indicate that successful clinical outcomes for patients are determined not only by the preference of empirical antibiotics but also by other important clinical factors.

The study shows that risk factors such as age over 65 years, comorbidities, initial symptoms during treatment, such as electrolyte disturbances, and severe pneumonia are associated with poor outcomes. Comorbidities that exacerbate the clinical outcome of CAP include chronic obstructive pulmonary disease, chronic heart disease, diabetes mellitus, malignancy, and cerebrovascular disease. Clinical manifestations such as pleural effusion, hypoxemia, respiratory failure, and electrolyte disturbances increase the risk of clinical deterioration.¹³ Other studies have identified factors that increase the risk of poor outcomes, including the etiology of CAP, disease severity, comorbidities, and the setting of care.¹⁴

CAP infections place a burden on society throughout the year, especially in patients with underlying chronic conditions. Individuals with COPD, asthma, smokers, chronic heart disease, and diabetes mellitus have been shown to have an increased risk of pneumonia compared to those without these conditions. These conditions can negatively impact patient outcomes, including increased short- and long-term mortality rates.¹⁵ Systematic reviews and meta-analyses show that comorbidities such as COPD, hypertension, and diabetes, as well as smoking risk factors, are associated with an increased risk of CAP. Comorbidities and smoking risk factors play an essential role in increasing the incidence, complications, and mortality of CAP.¹⁶ This is consistent with research findings that comorbidities such as pulmonary diseases, which affect the lungs, influence the clinical outcomes of patients with CAP.

The hospital rooms used in this study were ICU and non-ICU treatment. Significant differences were shown in the type of hospital room on patient outcomes (recovery or death). CAP patients admitted to the ICU had an in-hospital mortality risk of 17% and a 1-year mortality rate close to 50%. Patients with delayed ICU admission had a higher 6-month mortality rate than those who received immediate ICU care. Early identification of CAP patients is critical to determine the need for ICU/non-ICU care and potential mortality. Patients with low economic class increase the risk of CAP progression and in-hospital mortality.¹⁷ A retrospective cohort study showed the mortality rate of pneumonia patients in the ICU was 24%, in the hospital was 36%, and the mortality rate within 1 year was 60%.¹⁸

The culture results showed that *Klebsiella pneumoniae* bacteria were the most pathogenic bacteria causing CAP in this study. *Klebsiella pneumoniae* is a major cause of CAP and is associated with a high mortality rate (29.7% of patients died within 28 days) in Asian countries.¹⁹ *Klebsiella pneumoniae* is an important pathogen of respiratory tract infections that causes severe pneumonia and multiorgan infections.^{20,21} A 2022 study by Chen *et al.* in Taiwan showed that nosocomial pneumonia caused by *Klebsiella pneumoniae* infection, high SOFA (Severe Organ Failure Assessment) scores, and failure to receive appropriate definitive therapy were independent risk factors for mortality within 28 days.²²

The etiology of CAP is associated with worsening patient outcomes. *Streptococcus pneumoniae* is the most common pathogen causing CAP in both outpatient and inpatient settings, including non-ICU and ICU. *S. pneumoniae* is also associated with severe sepsis. *Haemophilus influenzae* is the second most common cause of CAP, especially in elderly patients. *Staphylococcus aureus* rarely causes CAP, but it is associated with poor clinical outcomes, particularly when caused by MRSA (methicillin-resistant *S. aureus*).¹⁴

Identification of the pathogen causing CAP can help select specific antibiotics and improve clinical outcomes, but in some cases, microbiological testing cannot be performed.¹⁴ This study showed that not

all patients had sputum culture and Gram examination. ATS/IDSA recommendations in 2019, Gram examination and sputum culture are performed on hospitalized patients with: (1) severe CAP, especially patients with intubation; (2) empirical therapy of MRSA (Methicillin-Resistant *S. aureus*) or *Pseudomonas aeruginosa*; (3) history of MRSA or *Pseudomonas aeruginosa* infection, especially respiratory tract infections; (4) history of hospitalization and receiving parenteral antibiotics in the last 3 months.⁶ Indications for culture and Gram examination in this study were in accordance with the 2019 ATS/IDSA recommendations, which were carried out in patients who met the criteria for severe CAP.

CAP patients with signs of organ dysfunction should be given empirical therapy as soon as the diagnosis is made. This aims to improve patient outcomes. Empiric therapy is given intravenously within the first 8 hours and given for 48 hours. The choice of empirical antibiotics is high-dose beta lactams that can eliminate pneumococci, *H. influenza*, *S. aureus*, and Enterobacter bacteria. Macrolide antibiotics can be added as empirical therapy in CAP patients with organ dysfunction. The combination of beta lactam antibiotics and macrolides can reduce mortality and macrolides can kill Legionella bacteria. If the patient shows clinical improvement and there is no atypical pathogen infection, macrolides can be discontinued after 3 days of administration. In CAP patients without signs of organ dysfunction, macrolide administration is optional. Research on macrolide administration showed no clear effect on patient outcomes.^{23,24}

The majority of antibiotic therapy given in this study was fluoroquinolone. The use of fluoroquinolone antibiotics can act against pathogenic bacteria that cause CAP, reduce mortality and therapy failure. Fluoroquinolone monotherapy also results in less frequent need for treatment discontinuation and minimal side effects of diarrhea. Systematic review and meta-analysis studies show fluoroquinolone antibiotic monotherapy is superior to β lactam, macrolide, or combination β lactam and macrolide antibiotics. Clinical success rates were significantly higher and adverse events were significantly fewer with fluoroquinolone monotherapy, with no significant difference in mortality.^{25,26}

Empirical antibiotics in this study predominantly did not meet the 2019 ATS/IDSA guidelines. The 2019 ATS/IDSA antibiotic recommendations for hospitalized patients with non-severe CAP use a combination of a beta-lactam and a macrolide, or monotherapy with a fluoroquinolone. Meanwhile, hospitalized CAP patients with severe symptoms can be given a combination of beta-lactam and macrolide antibiotics or a combination of beta-lactam and fluoroquinolone antibiotics. Although most patients in this study were not given antibiotics in accordance with the 2019 ATS/IDSA guidelines, the empirical antibiotics administered were consistent with other CAP treatment guidelines, namely the Management of Adult Community-acquired Pneumonia and Prevention-Update 2016 from Germany. Beta-lactam antibiotics, which can be supplemented with macrolides, are used for inpatients with moderate to severe CAP symptoms; alternative therapy is fluoroquinolones. In-patients with severe CAP

symptoms or organ dysfunction should be given a combination of beta-lactam and macrolide antibiotics as the drug of choice, with alternative therapy being fluoroquinolone antibiotics.²⁷

These findings support the concept that empirical antibiotics serve as initial therapy to control infection, but cannot stand alone as the main predictor of clinical outcomes. Optimization of comprehensive management, including early assessment of severity, management of comorbidities, and adequate supportive care, remains key to reducing mortality and length of stay.¹⁶ This study has limitations, including its observational design, which may introduce confounding factors that cannot be fully controlled. Further studies with a prospective design and larger sample sizes are needed to confirm these findings. Overall, this study shows that administering empirical antibiotics according to guidelines is not directly associated with reduced mortality or shorter hospital stays. In contrast, the type of care unit and comorbidities, such as lung disease, play a more dominant role.

Conclusion

Pneumonia can cause health problems, increasing hospitalization, morbidity, and mortality. Empirical antibiotic administration based on guideline can accelerate the length of hospitalization and significantly improve patient outcomes. In this study, the administration of empirical therapy in accordance with guidelines did not demonstrate a correlation with reduced duration of hospitalisation or decreased mortality. Nevertheless, a significant association was identified between ICU admission and comorbid lung disease, and patient outcomes.

Conflicts of Interest

There is no conflict of interest.

Funding sources

There is no funding source.

Acknowledgments

The author appreciatively acknowledges colleagues and friends who provided encouragement and assistance during this research.

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Exploration of The Knowledge and Lifestyles of Obese Housewives in Sukamaju Village

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ABSTRACT

Introduction: Housewives exhibit a higher susceptibility to obesity compared to women employed in office settings or those who are students, primarily due to the increased time spent at home attending to childcare responsibilities. The incidence of obesity is more prevalent among boys than girls, a trend that inversely correlates with the age of entering adulthood. At this stage, women are more prone to obesity than men. Married women experience weight gain at nearly twice the rate of their unmarried counterparts. Data from the 2011 and 2015 National Health and Morbidity Surveys (NHMS) indicate that the prevalence of obesity is greater in women than in men. Furthermore, the average Body Mass Index (BMI) of housewives surpasses that of individuals in other occupations. Obesity occurs when energy intake exceeds energy expenditure, resulting in an energy imbalance and subsequent weight gain, with 60% to 80% of this increase typically comprising body fat mass.

Methods: This quantitative study employed an observational design, utilizing univariate and bivariate analysis with the chi-square test for data analysis. The sampling technique implemented was simple random sampling.

Result: A significant association was identified between knowledge and obesity ($p = 0.028$). Additionally, a relationship between lifestyle and obesity was observed, with a p-value of 0.035.

Conclusion: A significant correlation exists between knowledge, lifestyle, and obesity among housewives.

Keywords: Knowledge; lifestyle; housewife; obesity



GREEN MEDICAL
JOURNAL
E-ISSN 2686-6668

Article history:

Received: 8 December 2023

Accepted: 10 December 2025

Published: 31 December 2025

Published by:

Faculty of Medicine
Universitas Muslim Indonesia

Address:

Jl. Urip Sumoharjo Km. 5, Makassar
South Sulawesi, Indonesia

Email: greenmedicaljournal@umi.ac.id

Introduction

Housewives are more susceptible to obesity than women who work in offices or are students because housewife spend more time at home taking care of their children⁽¹⁾. The prevalence of obesity in boys was higher than that in girls. This is inversely proportional to the age of entering adulthood. At this age, women are more likely to be obese than men. Married women gain weight almost twice as much as unmarried women⁽²⁾.

Obesity can occur when energy intake exceeds energy expenditure, causing an energy imbalance and impacting body weight, of which 60% to 80% is usually body fat mass⁽³⁾. The World Health Organization (WHO) defines obesity and excess weight as abnormalities or accumulation of excess fat that can endanger health. The body's metabolic processes produce energy that is greater than the calorie release⁽⁴⁾.

One of the nutritional problems faced by Indonesia is obesity or being overweight. Obesity or being overweight is characterized by an excessive nutritional status⁽⁵⁾. One indicator for determining nutritional status is the Body Mass Index (BMI), which is a simple index of body weight according to height. BMI is calculated by dividing an individual's weight in kilograms by the square of their height in meters (kg/m²). If an adult's BMI is more than 25, they are considered overweight, and if the BMI is more than 30, they are considered obese⁽⁶⁾. An increase in BMI causes obesity to develop into non-communicable diseases (NCDs) such as cardiovascular disease, diabetes mellitus, hypertension, etc.⁽⁷⁾.

Results from the 2011 National Health and Morbidity (NHMS) and 2015 NHMS surveys showed that the prevalence of obesity in women was higher than that in men. In addition, the average Body Mass Index (BMI) of housewives is higher than that of other occupations⁽⁸⁾.

Methods

This study used a quantitative research approach with an observational design and data analysis using univariate and bivariate analysis with the chi-square test. The sampling technique used was a simple random sampling technique. The sample size in this study was calculated using the Slovin formula.

Result

Table 1. Knowledge Frequency Distribution Results

Knowledge	Frequency	Percentage
Not enough	17	20.7
Currently	19	23.2
Good	46	56.1
Total	82	100

Based on the table above, information is obtained that out of 82 respondents used for research, on

knowledge, there are 17 respondents with a percentage of 20.7%, on moderate knowledge, there are 19 respondents with a percentage of 23.2%, and on good knowledge, there are 46 respondents with a percentage of 56.1%.

Table 2. Lifestyle Frequency Distribution Results

Lifestyle	Frequency	Percentage
Bad	61	74.4
Good	21	25.6
Total	82	100

Based on the table above, information was obtained that out of the 82 respondents used for the research, there were 61 respondents with a bad lifestyle, with a percentage of 74.4%, and with a good lifestyle, there were 21 respondents, with a percentage of 25.6%.

Table 3. Obesity Frequency Distribution Results

Obesity	Frequency	Percentage
Obesity 1	27	32.9
Obesity 2	55	67.1
Total	82	100

Based on the table above, information was obtained that out of 82 respondents used for the research, there were 27 respondents with obesity criteria 1 with a percentage of 32.9%, and there were 55 respondents with obesity criteria 2 with a percentage of 67.1%.

Table 4. Relationship between knowledge and obesity

Knowledge		Obesity		Total	P-Value
		Obesity 1	Obesity 2		
Not enough	n	5	12	17	0.028
	%	29.4%	70.6%	100.0%	
Currently	n	11	8	19	
	%	57.9%	42.1%	100.0%	
Good	n	11	35	46	
	%	23.9%	76.1%	100.0%	
Total	n	27	55	82	

%	32.9%	67.1%	100.0%
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Based on the table above, information was obtained that 17 respondents had less knowledge, with 5 respondents having obesity criteria 1 (29.4%) and 12 respondents having obesity criteria 2 (70.6%). Of the respondents with moderate knowledge, there were 19 respondents with details of 11 respondents having obesity criteria 1 with a percentage of 57.9% and 8 respondents having obesity criteria 2 with a percentage of 42.1%. There were 46 respondents with details of 11 respondents having obesity criteria 1 (23.9%) and 35 respondents having obesity criteria 2 (76.1%). The p-value obtained was 0.028.

Table 5. Relationship between lifestyle and obesity

Lifestyle		Obesity		Total	P-Value
		Obesity 1	Obesity 2		
Bad	n	24	37	61	0.035
	%	39.3%	60.7%	100.0%	
Good	n	3	18	21	
	%	14.3%	85.7%	100.0%	
Total	n	27	55	82	
	%	32.9%	67.1%	100.0%	

Based on the table above, information was obtained that 61 respondents had bad lifestyles, with 24 respondents having obesity criteria 1 (34.3%) and 37 respondents having obesity criteria 2 (60.7%). With a good lifestyle, there were 21 respondents, with 3 respondents having obesity criteria 1 (14.3%) and 18 respondents having obesity criteria 2 (85.7%). The obtained p-value was 0.035.

Discussion

Relationship between Knowledge and Obesity

This study was found that 17 respondents had insufficient knowledge, with 5 respondents having obesity criteria 1 and 12 respondents having obesity criteria 2. Of the respondents with moderate knowledge, there were 19 respondents with details of 11 respondents having obesity criteria 1 and 8 respondents having obesity criteria 2. There were 46 respondents with details of 11 respondents having obesity criteria 1 and 35 respondents having obesity criteria 2. This means there is a relationship between knowledge and obesity

Respondents with good knowledge were 46, with 11 respondents with obesity 1 and 35 respondents with obesity 2. Even though they have good knowledge, there are still many respondents who are obese. This is caused by internal and external factors. Internal factors include nutritional awareness. Even though respondents had good knowledge regarding obesity, if this knowledge is not implemented, it will cause the body to become obese; therefore, knowledge is not the main trigger of obesity. External factors are the questionnaire in the study, where the questionnaire only consists of 12 questions and are simple questions related to obesity, so it does not rule out the possibility that respondents in this study could answer well.

Knowledge is one component that can influence a person's lifestyle. People with limited knowledge, especially about nutritional issues, tend to lead unhealthy lifestyles and eating patterns, and vice versa. Consuming staple foods that are high in carbohydrates, if not accompanied by sufficient physical activity, can increase the risk of obesity⁽⁹⁾.

Everyone has different levels of knowledge; some are good, and some are lacking. According to Notoatmodjo, the following factors influence a person's knowledge: experience (can be obtained from one's own or other people's experience), level of education (can be a person's insight or knowledge), and information sources (such as the Internet, television, radio, newspapers, books, magazines, and books)⁽¹⁰⁾.

Apart from knowledge, nutrition awareness also has an influence on food choices. Nutritional awareness is a person's knowledge of the importance of consuming healthy and balanced food, food that is safe to consume, how to process food well, and how to live a healthy life⁽¹¹⁾.

This research is in line with Jaminah and Mahmudiono in 2018, who stated that there is a significant relationship between knowledge and the incidence of obesity with a value of $p = 0.03$ ⁽⁹⁾. Similar results were obtained by Mega Prima Pertiwi in 2022, which stated that there was a relationship between knowledge and central obesity with a value of $p = 0.026$ ⁽¹²⁾.

Relationship between lifestyle and obesity

In this study, respondents were obtained. There were 61 respondents had a bad lifestyle, 24 respondents included obesity criteria 1, and 37 respondents included obesity criteria 2. There were 21 respondents with good lifestyles, with criteria 3 respondents with obesity 1 and 18 respondents with obesity 2.

There were 21 respondents with a good lifestyle, with the criteria being three obese 1 respondents and 18 obese 2 respondents. Even though they had a good lifestyle, there were still many obese respondents. This is caused by both internal and external factors. Internal factors, namely changes in the estrogen hormone, a decrease in the estrogen hormone in women entering the pre-menopausal phase, triggers an increase in body weight due to lipogenesis. The external factor is the honesty of the respondents in answering the questionnaire.

Unhealthy lifestyles, especially dietary and physical activity patterns, can also cause obesity. A diet with excessive intake and sedentary physical activity can increase the risk of obesity because energy expenditure is not balanced with energy intake, thus causing excess body weight. Lifestyles are divided into positive and negative lifestyles. A negative lifestyle indicates a poor diet and low physical activity. A poor diet was defined as the habit of consuming sweet foods and drinks, fried foods, instant noodles, and snacks, not eating on time, and rarely consuming vegetables, fruit, and breakfast. Low physical activity patterns indicate a habit of infrequent exercise and sedentary lifestyle behaviors⁽¹³⁾.

In addition to an unhealthy lifestyle, hormonal changes can cause obesity. A decrease in the hormone estrogen affects the enzyme lipoprotein lipase, which reduces the amount of lipoprotein produced in the intestines and liver. This will affect lipid metabolism, decrease free fatty acid flux and fatty acid oxidation, and increase the incorporation of fatty acids into triglycerides. Women experience increased body weight and obesity due to increased fat synthesis or lipogenesis, resulting in increased Fat Mass (FM)⁽¹⁴⁾.

The results of this research are in line with Rika Kurniagustina in 2018, who stated that there is a relationship between diet and physical activity and obesity in class V children at SDN 01 Kalisari, East Jakarta with a value of $p = 0.033$ and 0.013 ⁽¹⁵⁾. The same results were also obtained by Ria Ramadani Wansyaputri in 2021, who stated that there was a significant relationship between diet and obesity with a value of $p = 0.013$, physical activity and the incidence of obesity with a value of $p = 0.020$ ⁽¹⁶⁾.

Conclusion

There was a significant relationship between knowledge and obesity and lifestyle and obesity, with p -values of 0.028 and 0.035 , respectively, according to the existing theory. However, the research results show that respondents who have good knowledge are still obese and a good lifestyle are still obese. Therefore, further research is required to produce more accurate findings. Socialization can be provided in the form of counseling, posters, and videos related to obesity.

Conflicts of Interest

The author declares that there is no conflict of interest in the conduct and preparation of this study. This research was carried out independently, without any personal or institutional interests that could have influenced the research process, including data collection, analysis, and interpretation of the findings.

Funding sources

This study did not receive any specific funding from public, commercial, or non-profit funding agencies. All costs associated with the implementation of this research were fully borne by the author.

Acknowledgments

The author would like to express sincere gratitude to all parties who contributed to the completion of this study. Special appreciation is extended to the academic supervisor for the guidance, support, and constructive feedback provided throughout the research process. The author also wishes to thank the local authorities of Sukamaju Village and all respondents, particularly the housewives who generously participated and provided valuable information for this study. Finally, the author is grateful to family members and colleagues for their continuous moral support, encouragement, and motivation during the completion of this thesis.

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Predictive Role of Non-Invasive Laboratory Markers in Hepatic Fibrosis among Hepatitis B Patients

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ABSTRACT

Introduction: Chronic hepatitis B (CHB) is a major cause of liver fibrosis, which may progress to cirrhosis if undetected. Non-invasive biomarkers such as Gamma-glutamyl Transferase to Albumin Ratio (GAR), Alkaline Phosphatase to Platelet Ratio (APPR), and Alkaline Phosphatase plus Gamma-glutamyl Transferase to Platelet Ratio (AGPR) have shown promise in predicting fibrosis severity, potentially outperforming traditional markers like APRI.

Methods: We conducted a cross-sectional study involving 34 CHB patients at Dr. Sardjito General Hospital, Yogyakarta (October 2022–February 2023). Liver stiffness was assessed using shear wave elastography (SWE) and staged according to the Metavir system (F0–F4). GAR, APPR, and AGPR were calculated from laboratory data. Spearman correlation and linear regression analyses were used to evaluate their association with fibrosis severity.

Result: AGPR showed the strongest correlation with fibrosis stage ($\rho = 0.611$, $p < 0.001$), followed by GAR ($\rho = 0.450$, $p = 0.008$) and APPR ($\rho = 0.384$, $p = 0.026$). All three indices were significant in univariate regression, while the combined model demonstrated improved predictive performance ($R^2 = 0.389$, $p = 0.003$) despite lack of independent significance in multivariate analysis.

Conclusion: GAR, APPR, and AGPR are promising non-invasive biomarkers for assessing liver fibrosis in CHB patients. Their combined use enhances diagnostic accuracy and offers practical benefits, particularly in settings where biopsy is not available.

Keywords: Chronic hepatitis B; Liver fibrosis; Non-invasive biomarkers; GAR; APPR; AGPR



GREEN MEDICAL
JOURNAL
E-ISSN 2686-6668

Article history:

Received: 25 September 2025

Accepted: 20 December 2025

Published: 31 December 2025

Published by:

Faculty of Medicine
Universitas Muslim Indonesia

Address:

Jl. Urip Sumoharjo Km. 5, Makassar
South Sulawesi, Indonesia

Email: greenmedicaljournal@umi.ac.id

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Introduction

Chronic hepatitis B virus (HBV) infection is one of the most serious global public health challenges, impacting an estimated 254 million people and causing over 1.1 million deaths each year owing to cirrhosis and hepatocellular carcinoma (HCC)⁽¹⁾. Hepatitis B prevalence is high in Southeast Asia, notably in Indonesia, with national seropositivity rates ranging from 7% to 10%, placing the country in the top ten worldwide in terms of HBV burden^(2,3). According to the Indonesian Ministry of Health, almost 18 million individuals are chronically infected with HBV. Chronic hepatitis B continues to be a major cause of liver disease morbidity in Yogyakarta's Special Region. Hospital-based research at Dr. Sardjito General Hospital found that HBV infection was the leading cause of hepatocellular carcinoma (HCC) in around 48% of cases, with most patients aged 46 to 55 years⁽⁴⁾. Despite this burden, complete screening for liver fibrosis is rare outside of tertiary care facilities, creating a diagnostic gap in early-stage disease diagnosis^(5,6).

Liver fibrosis is an important stage in the progression of HBV infection, where more extracellular matrix builds up, potentially causing portal hypertension, liver failure, and HCC^(3,7). While liver biopsy is still the gold standard for detecting fibrosis, it is invasive, expensive, and unsuitable for large-scale or repeated usage^(8,9). To address this, the World Health Organization (WHO) recommends using non-invasive tests like the AST to Platelet Ratio Index (APRI) and the Fibrosis-4 Index (FIB-4) as easier options, particularly in places with limited resources. However, these indexes have a few drawbacks^(10,11). Variable ALT levels during HBV infection reduce APRI's accuracy in diagnosing intermediate fibrosis (F2-F3), limiting its sensitivity to less than 60%^(8,9). FIB-4, although more accurate than APRI in certain cases, might exaggerate fibrosis in older persons owing to the inclusion of age in the calculation, and it may underrepresent cholestatic or synthetic liver dysfunction, limiting its value in early-stage HBV fibrosis^(10,12).

Given these constraints, new research has suggested novel HBV-specific laboratory indices that aim to improve diagnostic accuracy^(13,14). Among these, the Gamma-glutamyl Transferase to Albumin Ratio (GAR), Alkaline Phosphatase to Platelet Ratio (APPR), and Alkaline Phosphatase plus GGT to Platelet Ratio (AGPR) have been found to predict liver scarring more accurately, especially in Asian people^(15,16). For example, the AGPR has an area under the receiver operating characteristic curve (AUROC) of 0.83-0.87 for diagnosing severe fibrosis and cirrhosis in patients with chronic HBV, outperforming conventional markers such as APRI and FIB-4⁽¹⁶⁾. These measures also consider other liver function factors like ALP, GGT, and albumin, which indicate liver damage, the liver's ability to produce proteins, and high blood pressure in the liver^(17,18). These aspects are often neglected in traditional indices. Their simplicity, consistency, and utilization of regular blood markers make them promising candidates for widespread application, although comparative validation in HBV-endemic areas is limited^(15,16).

In the context of Indonesia's high HBV burden and limited access to liver biopsy or elastography at the

primary care level, there is an urgent need to develop additional reliable, low-cost, and HBV-specific non-invasive laboratory indicators that may be incorporated into normal clinical processes. This research, which will take place at Dr. Sardjito General Hospital and Universitas Gadjah Mada (UGM) in Yogyakarta, aims to evaluate how accurately GAR, APPR, and AGPR can predict liver fibrosis stages in patients with chronic hepatitis B. Yogyakarta, located in central Java, confronts comparable public health difficulties to other high-prevalence locations, making it an appropriate environment for investigating alternate fibrosis indicators. The results are likely to help create more context-appropriate diagnostic tools, minimize dependence on invasive procedures, and improve liver disease treatment in resource-constrained settings.

Methods

This observational analytic study with a cross-sectional design was conducted at Dr. Sardjito General Hospital, Yogyakarta, Indonesia, from October 2022 to February 2023. The study involved 34 adult patients diagnosed with chronic hepatitis B (CHB) who met the inclusion criteria of being aged 18 years or older, having a confirmed CHB diagnosis, and providing informed consent to undergo laboratory testing and liver stiffness assessment. Patients with co-infection by other hepatitis viruses (HCV or HDV), other chronic liver diseases, or severe coagulopathy were excluded. Venous blood samples were collected to measure gamma-glutamyl transferase (GGT), albumin, alkaline phosphatase (ALP), and platelet count using automated analyzers. Based on these laboratory values, three non-invasive indices were calculated: the Gamma-glutamyl Transferase to Albumin Ratio (GAR), the Alkaline Phosphatase to Platelet Ratio (APPR), and the Alkaline Phosphatase plus Gamma-glutamyl Transferase to Platelet Ratio (AGPR). Liver stiffness was measured using shear wave elastography (SWE) performed by two trained radiologists following standardized procedures, and fibrosis stages were categorized according to the Metavir scoring system (F0–F4). The median SWE value for each participant was used for staging, and inter-observer agreement was determined using Cohen's kappa coefficient. All laboratory and imaging procedures adhered to internal and external quality control standards.

Statistical analysis was performed using SPSS version 28.0 (IBM Corp., Armonk, NY, USA). Descriptive data were presented as mean \pm standard deviation or median (range) as appropriate. Spearman's rank correlation test was used to determine the relationship between GAR, APPR, AGPR, and fibrosis stage, while linear regression analyses were conducted to identify predictors of liver stiffness. A two-tailed p-value of <0.05 was considered statistically significant. Ethical approval was obtained from the Health Research Ethics Committee of the Faculty of Medicine, Universitas Islam Sultan Agung. Written informed consent was obtained from all participants prior to enrollment, and all procedures were carried out in accordance with the Declaration of Helsinki.

Result

This study included a total of 34 subjects with chronic hepatitis B who underwent laboratory testing and shear wave elastography (SWE) for liver fibrosis assessment. Subject characteristics are presented in **Table 1**. The mean age was 45.12 ± 14.2 , with males comprising most participants (61.8%). Laboratory results demonstrated mean values of GAR at 6.88 ± 5.28 , APPR at 0.58 ± 0.44 , and AGPR at 0.78 ± 0.61 , while fibrosis stages were distributed as follows: F0 (26.4%) F1 (5.8%), F2 (41.17%), F3 (17.3%), and F4 (8.8%), based on Metavir scoring.

Table 1. Characteristic Demographic

Variable	Value
Age (years)	45.12 ± 14.2
Body Mass Index (kg/m ²)	23.97 ± 3.9
Diagnosed Duration (years)	6.73 ± 5.32
Sex, n (%)	
Male	21 (62%)
Female	13 (38%)
Symptoms, n (%)	
Fever	3 (9%)
Jaundice	5 (14.7%)
RUQ pain	12 (35%)
Choluric urine	4 (11.7%)
Acholic stool	1 (2.9%)
Comorbidities, n (%)	
Alcohol consumption	0
Autoimmune disease	0
History of cholestasis	0
HIV infection	0
Chronic kidney disease (or renal failure)	2 (5.8%)
Hepatitis C virus (HCV) infection	0
Parental history of hepatitis B	9 (26.4%)
Hypertension	5 (14.7%)
Diabetes mellitus	2 (5.8%)
History of malignancy (or cancer)	0
Laboratories Examination Finding	
Eritrocyte	4.6 ± 0.92
Haemoglobin	13.37 ± 2.3
Haematocrit	40.51 ± 7.25
MCV	88.44 ± 8.21
MCH	94.77 ± 121.6

MCHC	33.02 ± 0.95
Leukocyte	6.23 ± 1.87
Trombocyte	196.41 ± 72.26
Liver Test Function	
Total Protein	7.55 ± 0.65
Globulin	3.22 ± 0.72
Albumin (g/dL)	4.39 ± 0.65
AST	35.52 ± 16.9
ALT	31.71 ± 14.84
Gamma GT	23.46 ± 13.49
ALP (u/L)	90.29 ± 29.7
Non – Invasive Biomarker	
GAR	6.88 ± 5.28
APPR	0.58 ± 0.44
AGPR	0.78 ± 0.61
Metavir Index (kPa)	7.24 ± 1.67
Liver Fibrosis Grade, n (%)	
F0	9 (26.4%)
F1	2 (5.8%)
F2	14 (41.17%)
F3	6 (17.3%)
F4	3 (8.8%)

Data source: primary data collected from study participants at Dr. Sardjito General Hospital, Yogyakarta (October 2022–February 2023).

A Spearman correlation analysis was conducted to assess the link between non-invasive indicators and liver fibrosis, with the results shown in **Table 2**. Of the three indices, AGPR had the most robust positive connection with liver stiffness (Spearman's $\rho = 0.46$, $p = 0.019$), followed by GAR ($\rho = 0.46$, $p = 0.006$) and APPR ($\rho = 0.29$, $p = 0.092$). These findings suggest a moderate to strong association between these biomarkers and the degree of fibrosis measured by SWE. Further analysis using simple linear regression revealed that all three biomarkers were significant predictors of liver stiffness individually (see **Table 3**). GAR had a B coefficient of 0.144 ($p = 0.011$), APPR had a coefficient of 1.388 ($p = 0.014$), and AGPR demonstrated the highest predictive value with a coefficient of 1.572 ($p < 0.001$), explaining 37.4% of the variance in fibrosis ($R^2 = 0.374$).

Table 2. Spearman Correlation Between Non-Invasive Biomarkers and Liver Fibrosis Stage

Variable	Spearman's rho (ρ)	p – value
GAR	0.46	0.006
APPR	0.29	0.092

AGPR

0.39

0.019

Data source: primary data collected from study participants at Dr. Sardjito General Hospital, Yogyakarta (October 2022–February 2023).

Figure 1 illustrates the receiver operating characteristic (ROC) curves of GAR, APPR, and AGPR for screening significant liver fibrosis ($\geq F2$) in patients with chronic hepatitis B based on shear wave elastography. Among the three non-invasive biomarkers, AGPR demonstrated the highest discriminative ability with an area under the curve (AUC) of 0.67, followed by GAR and APPR, both with an AUC of 0.64. Although the AUC values were within the acceptable range, these findings indicate that GAR, APPR, and AGPR may serve as useful preliminary screening tools to identify patients at higher risk of significant fibrosis, particularly in clinical settings where invasive procedures or advanced imaging modalities are not readily available.

Figure 1. ROC curves of non-invasive laboratory markers for identifying significant liver fibrosis ($\geq F2$).

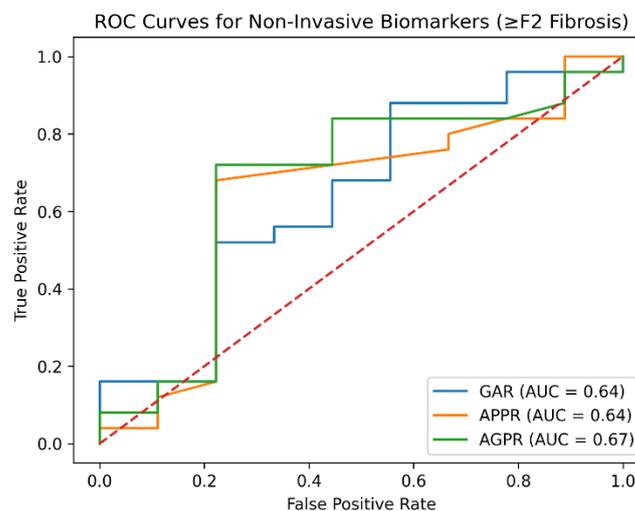


Table 3 summarizes the screening performance of GAR, APPR, and AGPR for identifying significant liver fibrosis ($\geq F2$), including the area under the curve (AUC), optimal cut-off values, sensitivity, and specificity. AGPR showed the highest overall discriminative performance (AUC 0.67) with an optimal cut-off value of 0.44, yielding a sensitivity of 72.0% and specificity of 77.8%. GAR demonstrated the highest sensitivity at 88.0% using a cut-off value of 3.21, albeit with lower specificity (44.4%), suggesting its potential utility as a sensitive screening marker. APPR showed a more balanced screening performance with an AUC of 0.64, sensitivity of 68.0%, and specificity of 77.8% at a cut-off value of 0.36. Overall, these serum-based indices provide a less invasive and easily accessible approach for fibrosis risk stratification rather than definitive diagnosis.

Table 3. Area Under the Curve (AUC) of GAR, APPR, and AGPR for Identifying Significant Liver Fibrosis ($\geq F2$)

Biomarker	AUC	Optimal Cut-off	Sensitivity (%)	Specificity (%)
GAR	0.64	3.21	88.0	44.4
APPR	0.64	0.36	68.0	77.8
AGPR	0.67	0.44	72.0	77.8

Discussion

This study assessed the predictive efficacy of three serum-based indices: Gamma-glutamyl Transferase to Albumin Ratio (GAR), Alkaline Phosphatase to Platelet Ratio (APPR), and Alkaline Phosphatase plus Gamma-glutamyl Transferase to Platelet Ratio (AGPR) in evaluating the severity of liver fibrosis in patients with chronic hepatitis B. Although none of the individual biomarkers demonstrated statistical significance in the multivariate linear regression model, their collective predictive strength was notable, with the combined model explaining 38.9% of the variance in fibrosis severity ($R^2 = 0.389$; $p = 0.003$). These findings suggest that the integrated use of multiple biomarkers may offer a more reliable and nuanced approach for non-invasive fibrosis evaluation.

The Spearman correlation analysis confirmed that all three indices had a statistically significant positive correlation with fibrosis stage, with GAR showing the strongest association ($\rho = 0.46$), followed by AGPR and APPR. This supports prior evidence indicating that gamma-glutamyl transferase (GGT) and alkaline phosphatase (ALP) levels are not only markers of cholestasis but also correlate with fibrotic progression in chronic liver disease. Albumin and platelet levels, commonly reduced in advanced liver disease, further enhance the discriminatory ability of these composite indices. The significant correlations found in this study are consistent with reports by Pan *et al.* (2022), who demonstrated that APPR could differentiate fibrosis stages in HBV-infected patients, and Li *et al.* (2022), who identified GAR as a prognostic factor in liver and biliary cancers ^(13,16).

This study supports prior evidence indicating that GGT and ALP levels reflect biliary injury and fibrotic progression, while decreases in albumin and platelets enhance discrimination in composite indices. Notably, Lu *et al.* (2017) reported that GAR significantly outperformed APRI and FIB4 in staging significant fibrosis and cirrhosis in chronic hepatitis B, with areas under the ROC curve (AUROC) of 0.82 vs. 0.70 for APRI and 0.68 for FIB4 ⁽¹⁵⁾. Furthermore, a comparative study of GPR and GAR demonstrated higher AUROCs than APRI in ruling out significant fibrosis (negative predictive value > 93%)(19). While comparisons between GPR and APRI/FIB4 were mixed in some cohorts, GAR displayed consistent superiority over APRI in both training and validation groups.

Although the univariate regression analyses revealed that each biomarker significantly predicted liver stiffness individually, particularly AGPR ($p < 0.001$), none of them retained significance in the multivariate model. This may reflect multicollinearity, where strong intercorrelations between predictors can obscure the independent contribution of each variable. Notably, this does not diminish the clinical utility of the model. Instead, it highlights the value of using a multiparametric approach, a strategy that has been increasingly endorsed in recent hepatology literature^(18,20).

The practical appeal of GAR, APPR, and AGPR lies in their use of routine laboratory values, making them cost-effective and widely accessible, especially in low-resource settings. Compared to other established non-invasive fibrosis scoring systems such as APRI, FIB-4, and FibroTest, these indices offer a potentially more liver-specific profile, integrating cholestatic and hepatocellular injury markers with hematologic parameters. Several recent meta-analyses and cohort studies have emphasized the growing role of composite biomarker panels in liver fibrosis screening and monitoring^(17,21).

Despite these strengths, our study has several limitations. The sample size was relatively small ($n = 34$), which may limit statistical power, especially for multivariate modeling. Moreover, liver fibrosis staging was based on shear wave elastography (SWE) rather than liver biopsy. While SWE is well-validated and non-invasive, its accuracy may still be affected by inflammation, hepatic congestion, or operator variability⁽²²⁾. Additionally, potential confounders such as metabolic syndrome components or viral load were not controlled in this model.

Future studies should aim to validate these findings in larger, diverse cohorts and explore the predictive value of GAR, APPR, and AGPR across different etiologies of liver disease, including non-alcoholic fatty liver disease (NAFLD) and hepatitis C. There is also growing interest in combining biochemical indices with machine learning algorithms or imaging biomarkers (e.g., radiomics, elastography features) to enhance diagnostic accuracy and fibrosis stratification.

Conclusion

In patients with chronic hepatitis B, the non-invasive laboratory indices GAR, APPR, and AGPR demonstrated acceptable discriminative ability for screening significant liver fibrosis ($\geq F2$), with AGPR showing the highest performance (AUC 0.67), followed by GAR and APPR (both AUC 0.64). GAR provided high sensitivity (88.0%), supporting its potential role as an initial screening marker, while AGPR and APPR showed more balanced sensitivity and specificity. Given their simplicity, low cost, and reliance on routinely available laboratory parameters, these indices may serve as less invasive adjunctive tools for fibrosis risk stratification, particularly in resource-limited settings where liver biopsy or advanced imaging modalities are not readily accessible. Further validation in larger and more diverse cohorts is warranted.

Conflicts of Interest

There is no conflict of interest.

Funding sources

This research did not receive any specific grant from funding agencies in the public, commercial, or non-profit sectors. The authors declare that there was no financial support influencing the study design, data collection, analysis, interpretation, or writing of the manuscript.

Acknowledgments

The authors would like to thank the medical and laboratory staff at Dr. Sardjito General Hospital, Yogyakarta, for their technical assistance in sample collection and data acquisition. We also acknowledge the support from the Department of Internal Medicine, Universitas Islam Sultan Agung, for providing the necessary facilities and general guidance throughout the study.

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Original Article

Open Access

Risk Factor and Symptoms of Back Pain in Coastal Fisherman in Jaya Bakti Village Banggai

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ABSTRACT

Introduction: Back pain is a significant global musculoskeletal health issue, particularly affecting occupational groups with high physical demands, such as fishermen. This study aimed to describe demographic factors (age), lifestyle (smoking, alcohol consumption), socioeconomic status, and accompanying symptoms associated with back pain in a population of coastal fishermen in Jaya Bakti Village, Pagimana, Banggai Regency.

Methods: This study employed a descriptive quantitative approach, collecting data through structured questionnaires. The study sample consisted of 62 fishermen selected from the population at the research site.

Result: Analysis of 62 respondents showed the majority were over 25 years old (40.3% aged 25-35; 50.0% aged >36 years). Lifestyle analysis in a sub-sample of 21 respondents revealed a very high prevalence of smoking (90.5%) and alcohol consumption in 38.1% of respondents. Income data from 41 respondents indicated the majority (63.4%) earned between IDR 500,000 until IDR 1,000,000 per month. 20 respondents reporting back pain, the most dominant accompanying symptoms were headache (90%) and reported loss of consciousness (85%). This finding is atypical for mechanical low back pain and may reflect misinterpretation of symptoms or other underlying conditions, requiring further clinical investigation, followed by pain radiating to the abdomen (60%).

Conclusion: This descriptive study concludes that back pain among fishermen in the study location tends to occur in older age groups and may be exacerbated by high smoking rates. The reported accompanying symptoms, particularly the high frequency of self-reported episodes suggestive of loss of consciousness or presyncope.

Keywords: Back pain; fishermen; occupational health; risk factors; symptoms



GREEN MEDICAL
JOURNAL
E-ISSN 2686-6668

Article history:

Received: 6 October 2025

Accepted: 21 December 2025

Published: 31 December 2025

Published by:

Faculty of Medicine
Universitas Muslim Indonesia

Address:

Jl. Urip Sumoharjo Km. 5, Makassar
South Sulawesi, Indonesia

Email: greenmedicaljournal@umi.ac.id

Introduction

Low Back Pain, especially Low Back Pain (LBP), is a global epidemic that affects the quality of life of millions of people and is the leading cause of years lived with disability (YLD) worldwide.^{1,2} This burden is not only individual but also social and economic, including direct health care costs and indirect costs due to decreased work productivity.³ Certain groups of workers, especially those involved in heavy manual work, are exposed to a higher risk of developing this musculoskeletal condition. Fishermen are one of the professions with a high risk of musculoskeletal disorders, including back pain. Characteristics of fishermen's work such as lifting heavy weights (nets, catches, ice), working in a hunched or awkward posture for long periods of time, exposure to whole-body vibration (WBV) from boat engines, as well as unstable working conditions due to boat movement at sea, all contribute to biomechanical stress on the spine.^{4,5,6} The accumulation of this exposure can lead to microinjuries, degeneration of the intervertebral discs, and muscle strain, which manifests as back pain.

In addition to occupational factors, individual and lifestyle factors also play an important role in the pathogenesis of back pain. Old age is consistently associated with an increased prevalence of back pain, often associated with degenerative changes in the spine.² Lifestyles such as smoking have been shown to be associated with an increased risk of back pain, possibly through mechanisms involving disc nutrition disorders and increased systemic inflammation.^{7,8} Alcohol consumption, especially in excessive amounts, can also affect bone and musculoskeletal health in general.⁹ Socioeconomic factors, such as income levels, can indirectly affect the risk of back pain through access to healthcare, working conditions, and nutritional status.¹⁰ Understanding the profile of back pain and related factors in specific populations such as coastal capture fishers is critical to designing effective prevention and management interventions. This research was conducted in Jaya Bakti Village, Pagimana District, Banggai Regency, a coastal community where the majority of the population depends on capture fisheries. This study aims to provide a descriptive picture of demographic characteristics (age), lifestyle (smoking, alcohol), income, and the type and frequency of comorbidity symptoms experienced by fishermen in this region who report back pain.

Methods

This observational analytic study with a cross-sectional design was conducted at Dr. Sardjito General Hospital, Yogyakarta, Indonesia, from October 2022 to February 2023. The study involved 34 adult patients diagnosed with chronic hepatitis B (CHB) who met the inclusion criteria of being aged 18 years or older, having a confirmed CHB diagnosis, and providing informed consent to undergo laboratory testing

and liver stiffness assessment. Patients with co-infection by other hepatitis viruses (HCV or HDV), other chronic liver diseases, or severe coagulopathy were excluded. Venous blood samples were collected to measure gamma-glutamyl transferase (GGT), albumin, alkaline phosphatase (ALP), and platelet count using automated analyzers. Based on these laboratory values, three non-invasive indices were calculated: the Gamma-glutamyl Transferase to Albumin Ratio (GAR), the Alkaline Phosphatase to Platelet Ratio (APPR), and the Alkaline Phosphatase plus Gamma-glutamyl Transferase to Platelet Ratio (AGPR). Liver stiffness was measured using shear wave elastography (SWE) performed by two trained radiologists following standardized procedures, and fibrosis stages were categorized according to the Metavir scoring system (F0–F4). The median SWE value for each participant was used for staging, and inter-observer agreement was determined using Cohen's kappa coefficient. All laboratory and imaging procedures adhered to internal and external quality control standards.

Research design

This study employs a quantitative descriptive research design to delineate the characteristics and frequency of the variables examined within the population of coastal capture fishermen in Jaya Bakti Village, Pagimana, Banggai Regency.

Setting and Sample/Participants

The research was conducted in Jaya Bakti Village, Pagimana District, Banggai Regency. The target population is coastal fishermen in the village. Sampling appears to use non-probability techniques such as convenience sampling. The number of respondents varied for the analysis of different variables: age data were analyzed from 62 respondents, lifestyle data (smoking and alcohol) from a sub-sample of 21 respondents, income data from 41 respondents, and symptom data accompanying back pain from a sub-sample of 20 respondents who specifically reported experiencing back pain. The inclusion criteria are likely to be active fishermen in Jaya Bakti Village, while the exclusion criteria are not mentioned in the source data. The difference in sample size between variables is a limitation that needs to be considered.

Measurement and Data Collection

Primary data were collected using structured questionnaire instruments that were distributed to fisher respondents. The questionnaire included a section on demographic data (age), lifestyle (smoking status, alcohol consumption), socioeconomic data (monthly income), and a specific section on symptoms that accompany back pain (pain radiating to the abdomen, loss of consciousness, headache, confusion) for the respondents who experienced it. This questionnaire appears to have been developed for this study, but information regarding the validity and reliability of the instrument is not available in the source data. Data is collected directly from respondents, possibly through structured interviews or self-filling. Reports of loss of consciousness were based solely on self-reported questionnaires and were not clinically verified.

Data analysis

The data collected from the questionnaire was processed and analyzed descriptively using absolute frequency and percentage calculations for each category of variables. The results of the analysis are presented in the form of frequency tables and narratives. No inferential statistical analysis (e.g., relationship or difference tests) was reported, in accordance with the descriptive objectives of this study. Data processing is likely to use basic statistical software or spreadsheets.

Ethical considerations

Although not explicitly stated, it is assumed that this study has considered ethical aspects. Oral or written consent should be obtained from each respondent following an explanation of the study's purpose. The confidentiality of respondent data is preserved. Information concerning approval from the research ethics committee is not included in the source data.

Result

The results of the descriptive analysis of the data collected from fishermen in Jaya Bakti Village are presented in the following tables and explained narratively.

Table 1. Age Distribution of Fisher Respondents (N=62)

Age	Quantity (f)	Percentage (%)
12-24 years old	6	9,7
25-35 years old	12	40,3
>36 years old	31	50,0
Total	62	100

Respondent Desa Jaya Bakti, 2024

Based on the analysis of age data from 62 respondents (see Table 1), it was determined that the population of fishermen is predominantly composed of adults and individuals in the advanced age group. Increasing age within the working population is associated with a higher risk of low back pain, mainly due to cumulative occupational exposure and degenerative changes, rather than elderly status. The majority of respondents (50.0%) were over 36 years old, followed by the 25-35 years old age group (40.3%). The youngest age group (14-24 years) is a minority (9.7%).

Table 2. Distribution of Fisher Respondents' Lifestyle (N=21)

Lifestyle Variables	Category	Quantity (f)	Percentage (%)
Smoking Status	Smoke	19	90,5
	No Smoking	3	14,3
	Total	21	100
Alcohol consumption	Drinking Alcohol	8	38,1
	Do Not Drink Alcohol	13	61,9
	Total	21	100

(Note: The percentage of smoking 14.3% for 'No Smoking' should be 9.5% for a total of 100%, but following the original data $3/21 = 14.3\%$)

Lifestyle analysis conducted on a sub-sample of 21 respondents (Table 2) showed a very high prevalence of smoking (90.5%). Regarding alcohol consumption, most of the respondents in this sub-sample (61.9%) stated that they did not drink alcohol.

Table 3. Distribution of Monthly Income of Fisher Respondents (N=41)

Revenue	Quantity (f)	Percentage (%)
IDR 0 – 500.000	6	9,7
IDR 500.000 – 1.000.000	12	40,3
>IDR 1.000.000	31	50,0
Total	62	100

Monthly income data, analyzed from 41 respondents (Table 3), showed that most fishermen (63.4%) had an income between Rp 500,000 to Rp 1,000,000.

Table 4. Distribution of Symptoms Participants in Fishermen with Back Pain (N=20)

Symptom questions	Answer yes (f)	Answer yes (%)	Answer no (f)	Answer no (%)
Does back pain radiate to the abdomen?	12	60,0	8	40,0
Experiencing loss of consciousness?	17	85,0	3	15,0
Experiencing Headache?	18	90,0	2	10,0
Are you confused?	5	25,0	15	75,0

Information on comorbidity symptoms was collected specifically from 20 respondents who reported

experiencing back pain (Table 4). More than half (60%) reported pain radiating to the abdomen. The most frequently reported accompanying symptoms were headache (90%) and episodes suggestive of loss of consciousness or presyncope (85%). Confusion was reported by 25% of respondents in this group.

Discussion

This descriptive research provides an initial overview of the profile of coastal fishermen in Jaya Bakti Village who are associated with back pain. The age distribution of respondents, with the majority being in the adult and advanced age groups (>36 years), is consistent with the literature showing an increased risk of back pain with age.² Natural degenerative factors in the spine as well as years of accumulated exposure to physical work, such as lifting weights and awkward postures prevalent in the fishing profession, likely contribute to the prevalence of pain in this age group.¹¹

The finding of a very high prevalence of smoking (90.5%) in the analyzed sub-sample is a significant aspect of lifestyle. The link between smoking and back pain, particularly chronic LBP, has been widely documented.^{7,8} Mechanisms that may be involved include disruption of microcirculation to the intervertebral disc due to nicotine, increased inflammatory mediators, and increased intra-discal pressure due to chronic cough.¹² Although this analysis was based on a small sub-sample (N=21), the high number highlights the potential for smoking as a relevant risk factor in this population. The prevalence of alcohol consumption (38.1%) was lower, and its association with back pain was less consistent in the literature, although heavy consumption may affect general musculoskeletal health.⁹

The majority of fishermen in the income study sample (N=41) were in the lower-middle income group. Socioeconomic status is often correlated with health conditions, including musculoskeletal pain.¹⁰ Lower incomes can limit access to healthcare, affect working conditions, nutritional status, and increase psychosocial stress, all of which can contribute to the risk or severity of back pain.¹³

Analysis of comorbidity symptoms in 20 fishermen who experienced back pain revealed an interesting clinical pattern. Pain that radiates to the abdomen/abdomen (60%) may indicate nerve root involvement (radiculopathy) or is referred pain of the spinal structure, requiring further diagnostic attention.¹⁴ High comorbidities with headache (90%) are often observed in chronic pain patients and may involve mechanisms such as central sensitization, secondary muscle tension, or stress.^{15,16}

The most unusual finding and requiring careful interpretation was the high number of reports of "loss of consciousness" (85%) associated with back pain. Syncope (fainting) is not a typical symptom of mechanical back pain. Potential explanations include vasovagal syncope due to severe pain, misinterpretation of the term by respondents (perhaps referring to presyncope or severe dizziness), or the presence of other underlying medical conditions.¹⁷ Given this very high percentage, further clinical validation is essential to rule out serious pathologies or "red flags".¹⁸ The confusion reported by 25% of

respondents could also be related to severe pain, medication side effects, or other factors associated with presyncope episodes.

Although not measured in detail, the employment context of fishers with exposure to vibration, weightlifting, and challenging work postures remains an important background that contributes to the risk of back pain in this population.^{4,6} It is worth acknowledging the limitations of this study, including descriptive design, sample size variations, potential bias in self-report data, and ambiguity in the interpretation of symptom terms. In addition, important occupational and psychosocial variables are not measured in detail.¹⁹

Conclusion

Descriptively, back pain among coastal fishermen in Jaya Bakti Village tends to occur in adult working-age groups, particularly those aged over 36 years, which may reflect cumulative occupational exposure rather than advanced age. A very prominent lifestyle factor is the high prevalence of smoking. Most fishermen have a lower-middle income level.

Among fishermen who experience back pain, the most common accompanying symptoms are headaches and pain radiating to the abdomen. The most notable finding requiring further attention is the high frequency of self-reported episodes suggestive of loss of consciousness or presyncope accompanying back pain. As these symptoms are atypical for mechanical low back pain, further clinical clarification and investigation are warranted to better understand their underlying causes in this population.

Conflicts of Interest

There is no conflict of interest.

Funding sources

This study was funded by the Faculty of Medicine, University Alkhairaat Palu, through its Internal Research Scheme. The sponsor had no involvement in the study design, data collection, analysis, or publication process.

Acknowledgments

The author would like to thank the Faculty of Medicine, ALkhairaat University for the support of the research facility.

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Comparison of Students Score between Progress Test and Final Test; Pilot Project

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ABSTRACT

Introduction: The implementation of diverse assessment methods has facilitated the collection of both quantitative and qualitative data, providing students with valuable feedback. Most programs reported that their assessment strategies were aligned with a competency framework, emphasizing constructive alignment and assessments structured according to Miller's pyramid. Many programs highlighted the significance of multiple low-stakes workplace-based assessments for evaluating real-world competencies, alongside the use of the final test, including progress testing in the knowledge domain to decrease student load. The aim of this study is to compare student final score between the progress test and the final test.

Methods: This is a mixed-method research. A quantitative of 506 students participated in the growth and development & geriatrics block, divided into two groups. Group A (progress test), comprising 253 students, underwent a progress test conducted over four exam sessions in 2024, as a pilot project. Meanwhile, Group B (final test), also with 253 students, completed a final test in 2023. The data from both groups were collected and analyzed using the T-independent test. Also, qualitative data was taken by student interviews.

Result: Group A, assessed in 2024, achieved a higher average score (69.33 ± 11.22) compared to Group B (54.92 ± 11.49). The T-independent test yielded a P value of <0.0001 , indicating a statistically significant difference. This suggests that the progress test method is more effective than the final test in enhancing students' final scores, as progress tests help alleviate cognitive load.

Conclusion: As a pilot initiative, the progress test has proven effective in improving students' final scores. It is recommended that this approach be extended to other educational blocks that have similar characteristics to the interventional blocks to enhance overall educational quality.

Keywords: Assessment; progress test; final test



GREEN MEDICAL
JOURNAL
E-ISSN 2686-6668

Article history:

Received: 19 June 2025

Accepted: 26 December 2025

Published: 31 December 2025

Published by:

Faculty of Medicine
Universitas Muslim Indonesia

Address:

Jl. Urip Sumoharjo Km. 5, Makassar
South Sulawesi, Indonesia

Email: greenmedicaljournal@umi.ac.id

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Introduction

In learning, the follow-up action that will be taken is to make a test and assess the results of the test, to assess how much the student understands in capturing this knowledge. The progress test is usually administered to all students in the medical program at the same time and at regular intervals (usually twice to four times yearly) throughout the entire academic program. The test samples the complete knowledge domain expected of medical students on completion of their course, regardless of the year level of the student. The resultant scores provide longitudinal, repeated measures, curriculum-independent assessment of the objectives of the entire medical program.¹

The progress test (PT) has been known in the world of education as a tool to measure competence. The test was originally held in Missouri and Maastricht in the 70s and has now been widely embraced in various countries. There are several medical education institutions in Indonesia, both public and private, that organize PT. The implementation of the PT has challenges. The challenge comes from the logistics of questions, time, energy, individual feedback, and problem analysis. The COVID-19 pandemic is also a challenge in itself, but it provides an opportunity to hold online universities and flexibility for university organizers and students.²

Progress tests can be a means for medical institutions to evaluate the progress of mastery of each scientific topic related to the field of medicine from all students by comparing changes in the progress test scores of each student from year to year. The implementation of the progress test is expected to make students have a good quality of knowledge so that later students will be able to pass the UKMPPD one-shot exam and are ready to enter the clinic station (co-ass).³

So far, there is still little research related to the relationship between progress test scores and final tests, The purpose of this study is to find out the comparison of Student Final Score Achievement between progress test and final test methods at the Faculty of Medicine, UMI Makassar as a pilot project.

Methods

This research is a mixed method using stratified sampling that collect in the data of block score in preclinical student and qualitative data through interview. A total of 506 sample students participated in the growth and development & geriatrics block, divided into two groups. Group A, comprising 253 students, underwent a progress test conducted over four exam sessions in 2024, while Group B, also with 253 students, completed a final test in 2023. The data from both groups were collected and analyzed using the T-independent test.

Result

This research consists of quantitative and qualitative data. There were a total of 506 students who took the Growth and development & geriatrics block, then divided into 2 groups. Group A with 253 students in 2024, with a progress test. The progress test in question is an exam that is divided into 4 sessions of 25 questions each. The questions in each exam are different. Then compared with group B with 253 students in 2023, with a final test of 100 question numbers.

Table 1. Student Score

	Group A	Group B
Score	student (%)	Student (%)
A	157(62)	13(5,1)
A-	35(13,8)	14(5,5)
B+	22(8,6)	18(7,1)
B	17(6,7)	37(14,6)
B-	9(3,5)	37(14,6)
C+	8(3,1)	33(13)
C	5(1,9)	35(13,8)
E	10(3,9)	66(26)

The highest score for progress test students was A (62%), followed by A- (13.8%) and B+ (8.6%). different between groups in the final test, the highest scores are B and B-. This provides information that progress scores are able to increase student grades by splitting the course material.

Group A, assessed in 2024, achieved a higher average score (69.33 ± 11.22) compared to Group B (54.92 ± 11.49). The T-independent test yielded a P value of <0.0001 , indicating a statistically significant difference. This suggests that the progress test method is more effective than the final test in enhancing students' final scores, as progress tests help alleviate cognitive load.

The results of the group A interview consisted of questions regarding the level of satisfaction with the progress test, whether they were very satisfied, satisfied, quite satisfied, less satisfied and dissatisfied. The five subjects were quite satisfied and one less satisfied with the following details below

Table 2. Student Interview

Subject	level of satisfaction	Reason of satisfaction level	Advantages	Disadvantages	Recommendation
1st	quite satisfied	because exams were held	Study more focus on	More frequent exam	Agree to continue

		every week	split exam		
2 nd	quite satisfied	Scores got better	Weekly study was better	Not easy to focus	Agree to continue
3 rd	quite satisfied	Could be more focus	Study time more frequent	More difficult questions	Agree to continue
4 th	quite satisfied	Less study time	Split exam got better	More frequent learning	Agree to continue
5 th	less satisfied	Unsatisfactory score	Deduce student load	Schedule of exam is more frequent	Agree to continue
6 th	quite satisfied	Reduce the burden of study	Focus on several materials	Must study hard	Agree to continue

The interview results showed that 6 students were not very satisfied because there were still several shortcomings. The tight lecture schedule makes the frequency of exams more than 4 times troublesome. On the other hand, there are also those who are satisfied because the student load can be reduced and feel more focused when split. Everyone agrees that the progress test will continue to the next blocks with improvements.

Discussion

Progress test in medical science is an assessment method where all students take the same exam, with the standards set by a new doctor expected to be competent. At Peninsula Medical School, each progress test consists of 125 multiple-choice questions with clinical vignettes and five answer options.⁷ The same question type was also used in this study.

Another study shows that final-year students, who have received more block material, are already familiar with the expected level of knowledge at the end of the undergraduate medical program.⁸ Based on the results in Table 1, progress test students achieved more satisfactory grades (A, A-, B+). Dividing the 100-item exam into four sessions of 25 questions reduces cognitive load and enhances focus.⁹ Progress tests are designed to evaluate long-term retention of knowledge rather than short-term memorization. They assess the breadth of a student's understanding of core medical knowledge, which is critical for the development of clinical competencies. Progress testing was found to be more reliable in evaluating retention of knowledge over time compared to traditional exams.¹⁰

The interview results showed differences in student perceptions. Some students felt burdened by frequent exams, while others felt more focused and experienced reduced cognitive load. Longitudinal studies in Germany show that repetitive progress testing is associated with learning progression and

performance in national high-stakes examinations. Repeated testing supports deeper learning, knowledge retention, and reduces surface learning ahead of examinations.¹¹⁻¹³ Progress tests often include detailed feedback, allowing students to reflect on their performance, identify weaknesses, and target areas for improvement. This encourages active learning and self-directed study, which are crucial skills in medical practice. This study highlighted how feedback from progress testing enhanced medical students' self-reflection, leading to more focused and effective study habits.¹⁴

A progress tests are relevant for preparing students for the national exit exam (UKMPPD), which uses CBT. Progress tests enable early identification of students with poor performance and guide institutions in offering academic remediation before students enter the clinical phase.¹³ Institutions can use progress test data to monitor student readiness, detect stagnation, and design targeted learning interventions.¹⁶

A key principle of the progress test is its longitudinal feedback function, which promotes deeper learning.¹⁷ Feedback from progress tests also contributes to quality control for item authors, lecturers, and curriculum committees by highlighting item reliability and performance across multiple test cycles.⁶ Repeated cycles of testing, feedback, and learning are known to enhance knowledge retention and strengthen transfer of learning in academic and clinical contexts.¹³⁻¹⁷

Unlike high-stakes exams, progress tests typically have a lower impact on final grades, which reduces test anxiety. This shift from pressure-based assessments to ongoing evaluations allows for a more holistic approach to learning and provides a less stressful environment for students to demonstrate their knowledge. Students who participated in progress testing reported lower levels of anxiety compared to those who relied on traditional high-stakes exams.¹⁸

Overall, progress test scores are also an important indicator for institutions to improve quality assurance. Providing item writers with reliability data from repeated test cycles helps identify strengths and weaknesses in item construction. These components support a programmatic assessment approach, integrating multiple assessment modalities to optimize student learning, ensure curriculum quality, and improve educational decision-making.¹⁵⁻¹⁷

Conclusion

As a pilot study, the progress test provided more satisfactory results compared to the final test. Progress tests can also be part of programmed assessment which is an integral approach of the assessment system to optimize learning functions, student decision making, and curriculum quality assurance.

Progress test could reduce student load. However, there are also those who think that the frequency of exams is a burden on students. It is recommended that this program be continued for further analysis.

Among fishermen who experience back pain, the most common accompanying symptoms are headaches and pain radiating to the abdomen. The most notable finding requiring further attention is the high frequency of self-reported episodes suggestive of loss of consciousness or presyncope accompanying back pain. As these symptoms are atypical for mechanical low back pain, further clinical clarification and investigation are warranted to better understand their underlying causes in this population.

Conflicts of Interest

There is no conflict of interest.

Funding sources

There is no funding source

Acknowledgments

There is no acknowledgment

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Preventable Risk Factor of Glaucoma

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ABSTRACT

Introduction: Glaucoma contributes of cases of number of irreversible blindness worldwide, with estimates reaching 112 million cases by 2040. About 50% remain unaware in the early stages of this disease unless there is already a visual disturbance or an acute attack.

Methods: This is an observational literature review. This study uses the PubMed and Google Scholar databases. The keywords searched were: Glaucoma risk factors, retinal ganglion cell damage, intraocular pressure, neuroprotection for glaucoma, metabolic disease and glaucoma. The inclusion criteria were original cohort studies, case-control studies, Randomized Controlled Trial (RCT), systematic review, and meta-analysis in the last decade in English. Non-English articles were excluded.

Results: The main preventable risk factors of glaucoma are increased intraocular pressure, oxidative stress, and metabolic syndrome. for every 1 mmHg increase in intraocular pressure there will be a loss of retinal nerv fiber layer of ~0.05 μ m to ~0.13 μ m per year. Controlling intraocular pressure with medications or laser/surgery can reduce intraocular pressure by 20-70%. Oxidative stress damage retinal ganglion cell particularly in normo-tension glaucoma, regardless of intraocular pressure. Metabolic syndrome increases oxidative stress thereby exacerbating retinal ganglion cell damage. The use of citicoline and nicotinamide has been widely proven to slow down retinal ganglion cell damage in glaucoma. The relationship between blood pressure with the progression of glaucoma is still debated.

Conclusion: Preventing the progression of glaucoma is important by controlling the preventable risk factors, including increased intraocular pressure, oxidative stress and metabolic syndrome. By decreasing intraocular pressure, damage to retinal ganglion cells slows down. Oxidative stress damages retinal ganglion cells regardless of intraocular pressure. Metabolic syndrome increases oxidative stress, thereby exacerbating retinal ganglion cell damage.

Keywords: Glaucoma; intraocular pressure; oxidative stress



GREEN MEDICAL
JOURNAL
E-ISSN 2686-6668

Article history:

Received: 1 September 2025
Accepted: 19 December 2025
Published: 31 December 2025

Published by:

Faculty of Medicine
Universitas Muslim Indonesia

Address:

Jl. Urip Sumoharjo Km. 5, Makassar
South Sulawesi, Indonesia

Email: greenmedicaljournal@umi.ac.id

Introduction

Glaucoma is one of the leading causes of blindness worldwide, ranking first as a cause of irreversible blindness. In the age range above 40 years, the number of glaucoma sufferers is generally around 3.5%. This number is estimated to reach around 112 million people by 2040. Glaucoma is a disease that causes damage to retinal ganglion cells, resulting in decreased visual acuity. Approximately 50% of glaucoma sufferers are unaware of this condition in the early stages until vision loss or an acute attack occurs. Primary Open Angle Glaucoma (POAG) has the highest incidence compared to other subtypes¹.

Glaucoma risk factors are multifactorial. There are both preventable and non-preventable factors. The non-preventable risk factors of glaucoma were identified, including a family history, anterior chamber depth, corneal thickness, axial length, myopia or hyperopia, advanced age, race, and gender. This article will discuss the main preventable glaucoma-related factors to achieve optimal treatment results, including increased intraocular pressure, oxidative stress, hypertension and metabolic syndrome^{2,3}.

Methods

This study is an observational literature review. This study used PubMed and Google Scholar databases. The keywords searched were: Glaucoma risk factors, retinal ganglion cell damage, intraocular pressure, neuroprotection for glaucoma, metabolic disease and glaucoma. The inclusion criteria were original cohort studies, case-control, Randomized Controlled Trial (RCT), systematic review, and meta-analysis in the last decade in English. Non-English articles were eliminated. The author carefully reviewed the selected articles to examine the topic.

Review and Discussion

Intraocular Pressure

Intraocular pressure (IOP) is determined by the production and disposal of aqueous humor, which is produced by the nonpigmented ciliary body. The lamina cribrosa, which functions to support Retinal Ganglion Cells (RGCs) as they exit the eyeball, is very vulnerable to changes in IOP. When IOP increases, the lamina cribrosa will experience pressure and RGC damage will occur. In addition to mechanical damage, high IOP will also disrupt the blood supply to the optic nerve, causing the optic nerve to lack nutrition. In addition, increased IOP will produce glutamate which will trigger Reactive Oxygen Species (ROS) which cause oxidative stress that ends in mitochondrial damage and cell damage. Therefore, in individuals with neurotrophic deficiencies will be more sensitive to a slight increase in IOP. Every 1 mmHg increase in IOP, there will be a loss of Retinal Nerv Fiber Layer (RNFL) of $\sim 0.05\mu\text{m}$ per year in

general, and $\sim 0.13\mu\text{m}$ in progressive cases. Thus, IOP control is the most important factor in the management of glaucoma. The normal IOP target is 10-21 mmHg⁴.

Treatment to achieve the IOP target can be with drugs or laser/surgery. Classes of drugs that are used include prostaglandin analog (increase aqueous humor outflow through the uveoscleral pathway), beta-blockers (reduce aqueous humor production by the ciliary body), alpha-adrenergic agonists (reduce aqueous humor production and improve outflow through the uveoscleral pathway), oral carbonic anhydrase inhibitors (CAI), and mannitol or glycerol (for acute glaucoma attacks)⁴.

If drug therapy is insufficient or laser facilities are available, so interventions may be necessary. Argon laser (ALT) and especially Selective Laser Trabeculoplasty (SLT) improve trabecular drainage and can lower IOP by 20-30%. A study conducted over six years, presented at the annual meeting of the American Academy of Ophthalmology (AAO) in 2024, found that with selective laser trabeculoplasty therapy, POAG experiences 29% slower progression compared to using eye drops. Previous studies found that selective laser trabeculoplasty is equally effective as eye drops. AAO recently published the results of an Ophthalmic Technology Assessment of selective laser trabeculoplasty, stating that this laser therapy can be used as a primary treatment for POAG, allowing most patients to be free of glaucoma eye drops, or in combination with eye drops. However, SLT's effectiveness decreases over time, with IOP control reaching 70% at 6 months post-procedure, and then dropping to 27% after 2 years. This procedure can be repeated⁵.

MIGS (Minimally Invasive Glaucoma Surgery), provides faster recovery and lower risks in POAG. MIGS uses micro-invasive procedures such as *iStent*, *Hydrus*, *CyPass*, or excimer laser trabeculostomy. This procedure increases aqueous humor outflow through the trabecular meshwork and reduces the risk of fibrosis. This procedure is intended for POAG, especially for mild to moderate degrees. One study showed a reduction in IOP of $>20\%$ over a four-year period and reduced the need for glaucoma medications. This procedure is very safe and can be combined with cataract surgery. The combination of MIGS and phacoemulsification can reduce the need for glaucoma eye drops⁶.

Trabeculectomy and drainage Implants are creating a fluid outflow pathway through the sclera into the subconjunctival space in advanced cases. This procedure is used when laser treatment is ineffective on primary or secondary open-angle glaucoma. The risks of trabeculectomy include bleb leakage, postoperative fibrosis, infection, and hypotonic maculopathy. The incidence of bleb leakage, hyphema, and hypotonic maculopathy after drainage implants is lower compared to trabeculectomy, but there is a greater risk of concurrent cataracts, diplopia/strabismus, and tube erosion. The success rate of both procedures is about 70-90%⁷.

Laser Peripheral Iridotomy (LPI) is the first-line therapy for angle-closure glaucoma. Generally used for angle-closure glaucoma with pupillary block, by making a small hole in the iris so that aqueous humor can flow to the anterior chamber. LPI can prevent acute angle-closure glaucoma attacks and prevent the adhesion of the iris to the trabecular meshwork. In a study using Spectral Domain Anterior Segment Optical Coherence Tomography (SD AS-OCT) on 22 eyes that underwent laser iridotomy, an increase in Angle Opening Distance (AOD), Trabecular Iris Space Area (TISA), Anterior Chamber Depth (ACD), Anterior Chamber Width (ACW), and Anterior Chamber Area (ACA) was found after one week of laser iridotomy. The effectiveness of LPI is about 65-70% in reducing IOP⁸.

Oxidative Stress

Oxidative stress occurs when there is an imbalance between free radicals and antioxidants. Oxidative stress results in impaired tissue stabilization, DNA and protein damage, and particularly damage to cells in the trabecular meshwork, optic nerve head, lamina cribrosa, and RGCs, which are responsible for glaucoma progression, particularly in glaucoma with normal IOP. Glaucoma with increased IOP also involves increased glutamate, which triggers ROS and cell damage, leading to apoptosis through the caspase pathway (a protease that breaks down cells). The NADPH Oxidase (NOX) enzyme is also involved in producing ROS in response to inflammation. Damaged mitochondria produce ROS, which further exacerbates mitochondrial damage. In addition to directly causing RGCs apoptosis, ROS can also induce RGCs apoptosis through NF- κ B activation (an inflammatory response). One study found that antioxidants such as glutathione, superoxide dismutase, and catalase decreased, accompanied by increased oxidative stress markers such as MDA (lipid damage) and nitrotyrosine in the serum and tears of glaucoma patients. Controlling oxidative stress is a new therapeutic target, alongside controlling IOP in glaucoma patients. One of the agents that is currently being researched a lot is citicoline, nicotinamide (vitamin B3), and vitamin D3 supplementation, which are neuroprotective compounds that can protect the structure and function of neurons, and indirectly can reduce the negative impact of oxidative stress⁹,

¹⁰.

Citicoline is a precursor for the synthesis of phosphatidylcholine and sphingomyelin, which are then useful in repairing RGCs membranes and optic nerve axons damaged by oxidative stress or chronic ischemia. This is important for reducing the vulnerability of RGCs to mechanical stress such as increased IOP. In vitro studies have found that citicoline prevents cell membrane damage and apoptosis of RGCs caused by oxidative stress. Citicoline increases levels of acetylcholine, dopamine, and serotonin in the central nervous system. This increase in neurotransmitters helps improve overall visual function. A study of Pattern Electroretinogram (PERG) and Visual Evoked Potentials (VEP) showed improvements in

glaucoma patients receiving citicoline therapy. An experimental study found that citicoline supplementation reduced mitochondrial dysfunction, a major pathway for RGCs death. Citicoline also increases glutamate uptake by astrocytes, decreases NMDA activity, and increases glutamate transporter expression. Citicoline has anti-apoptotic effects through modulating the expression of anti-apoptotic proteins (Bcl-2) and decreasing the expression of pro-apoptotic proteins (Bax, caspase-3). These effects reduce the progressive degeneration of RGCs and increase the survival of retinal neurons exposed to chronic stress due to elevated IOP. Citicoline also improves neuroplasticity by supporting the expression of neurotrophic factors such as Brain-Derived Neurotrophic Factor (BDNF) which is important for the regeneration of the visual pathway. In a clinical study, it was found that glaucoma patients who received long-term citicoline therapy experienced improvements in visual function and slowed visual field decline. In several studies, it was found that adjuvant therapy with citicoline can improve visual fields. In a study, oral administration of citicoline 500 mg/day with a treatment cycle of 120 consecutive days, followed by a 60-day break, for 2 years was reported to slow the decline in RNFL and Ganglion Cell Complex (GCC) thickness, as well as improve visual fields. In a study of the administration of 2% liposomal citicoline drops as an adjunct therapy in POAG patients, retinal function was improved and glaucoma progression was reduced¹¹⁻¹³.

Nicotinamide (vitamin B3) is a precursor of Nicotinamide Adenine Dinucleotide (NAD⁺). NAD⁺ is a coenzyme that helps improve optic nerve mitochondrial dysfunction, increasing cellular energy reserves (ATP), reducing oxidative stress, and increasing resistance to oxidative stress. Clinical trials are currently being conducted on the use of nicotinamide as a neuroprotector for the management of glaucoma in many countries. In a laboratory study, oral administration of nicotinamide resulted in 93% of the samples not developing glaucoma. Additionally, in a randomized controlled study involving 32 individuals with open-angle glaucoma, it was found that oral supplementation with calcium pyruvate 3 grams/day for 9 weeks led to an average increase of 8 test locations in the visual field compared to placebo. In line with this research, a 12-week clinical trial in Australia with 57 participants receiving nicotinamide supplementation of 3 grams/day found an improvement in retinal function assessed by electroretinography. One study found that the combination of nicotinamide and pyruvate improved short-term visual function in glaucoma patients already receiving IOP-lowering therapy. However, longer-term trials are needed to assess broader effects.¹⁴⁻¹⁶

Vitamin D3 has also been shown to influence aqueous humor production and outflow through the trabecular meshwork. Vitamin D3 acts through the vitamin D receptor (VDR), which interacts with the TGF- β 2/SMAD pathway in trabecular meshwork cells. VDR activation can inhibit SMAD2/3 phosphorylation and reduce the expression of profibrotic genes (such as fibronectin, α -SMA, and

collagen). This has the potential to reduce excessive ECM deposition, decrease resistance to aqueous humor outflow, and ultimately lower IOP. Experimental studies have shown that vitamin D3 reduces ECM remodeling and oxidative stress in TM cells. In animal models, vitamin D3 can lower IOP, reduce RGCs loss, and provide a protective effect on the optic nerve. Furthermore, vitamin D3 has a neuroprotective effect on the optic nerve. A study in monkeys found that vitamin D3 supplementation can reduce intraocular pressure. However, the benefits of vitamin D supplementation for glaucoma are still controversial and require further research.^{17,18}

High Blood Pressure

Elevated IOP and diminished ocular perfusion have been proposed as contributing factors to the development of optic neuropathy in glaucoma. Arterial blood pressure (BP) may modulate both parameters. Elevated BP has the potential to increase IOP through enhanced aqueous humor production, whereas hypotension may compromise ocular perfusion pressure (OPP), predisposing the optic nerve to ischemic injury. This complex interaction among IOP, OPP, and systemic BP is of particular clinical relevance, given the frequent co-occurrence of glaucoma and hypertension in aging populations¹⁹.

Elevated blood pressure has been shown to affect IOP through two main mechanisms. First, elevated blood pressure increases capillary pressure within the ciliary body, thereby increasing aqueous humor production. Second, elevated blood pressure increases episcleral venous pressure, thereby inhibiting aqueous humor outflow. Optic nerve damage occurs due to mechanical and ischemic compression of the nerve fibers. Although the eye has autoregulatory mechanisms to maintain consistent perfusion, elevated endothelin-1 levels in hypertensive individuals can disrupt vascular homeostasis, thereby impairing the regulation of ocular blood flow²⁰.

However, the correlation between blood pressure and glaucoma remains controversial. A study in Turkey showed that individuals with hypertension had significantly higher intraocular pressure (IOP) compared with normotensive subjects. Subsequent reductions in blood pressure were associated with a significant reduction in IOP in hypertensive patients. These observations suggest that poorly controlled systemic hypertension may contribute to persistent elevations in IOP, thereby increasing the progression of glaucomatous optic neuropathy. In contrast, some studies have found no significant association between blood pressure and increased IOP. Interestingly, other research suggests that in younger individuals, hypertension may have a positive effect by increasing ocular perfusion pressure (OPP), potentially reducing the risk of glaucoma. Furthermore, individuals receiving antihypertensive therapy have been reported to have a two to threefold increased risk of developing glaucoma. This association may be related to the nocturnal administration of antihypertensive medications, which can lead to

excessive drops in nighttime blood pressure and, consequently, a reduction in OPP^{21,22}.

Metabolic Syndrome

Metabolic syndrome (MetS) is a cluster of metabolic abnormalities including central obesity, hyperglycemia, hypertension, and dyslipidemia. Its prevalence continues to increase and is associated with an increased risk of various diseases, including glaucoma. Insulin resistance, a core component of MetS, has been hypothesized as a potential pathophysiological link between MetS and glaucoma. Several studies have investigated the relationship between MetS and GON in individuals diagnosed with glaucoma²³.

The brain contains high densities of insulin and insulin-like growth factor-1 (IGF-1) receptors. Disruption of these signaling pathways due to insulin resistance disrupts neuronal communication and activates pro-inflammatory processes, ultimately leading to RGC degeneration. Furthermore, insulin resistance has been shown to impair cerebral blood flow and increase oxidative stress, cause microvascular dysfunction (vasculopathy), and accelerate neurodegenerative mechanisms, further contributing to optic nerve damage and the development of glaucoma. Inflammatory mediators involved include TNF-alpha, IL-1 β , and nitric oxide. A study by Lee et al. found that MetS influences the incidence of POAG regardless of IOP.^{23,24}

Conclusion

The main preventable risk factors for glaucoma include increased intraocular pressure, oxidative stress, and metabolic syndrome. Every 1 mmHg increase in intraocular pressure there will be a loss of retinal nerve fiber layer of $\sim 0.05\mu\text{m}$ to $\sim 0.13\mu\text{m}$ per year. Intraocular pressure decreases by 20-70% with medication therapy or laser/surgery. Oxidative stress damage ganglion cell particularly in normo-tension glaucoma, regardless of intraocular pressure. Metabolic syndrome increases oxidative stress thereby exacerbating retinal ganglion cell damage. The use of citicoline and nicotinamide to decrease oxidative stress is supported by many studies. As for the routine administration of vitamin D, it remains controversial. The relationship between blood pressure and glaucoma is still debated.

Conflicts of Interest

There is no conflict of interest.

Funding sources

There is no funding source.

Acknowledgments

There is no acknowledgments.

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