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PHARMACOLOGICAL AND NON-PHARMACOLOGICAL PREDICTORS OF MORTALITY (WITHIN 6 MONTHS) FOR PATIENTS PRESENTING WITH STROKE.

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Abstract:

Background: Stroke is one of the major health burdening causes of mortality and morbidity worldwide, especially during the first 6 months of stroke onset. Early detection of the predictors of mortality can improve outcomes.

Objective: Examine pharmacological and non-pharmacological determinants for the six-month mortality in patients hospitalized due to ischemic stroke.

Methods: This is a cohort study which carried out in Basra Teaching Hospital. The prospective cohort study lasted six months. in 2024. 120 adult patients with stroke (ischemic) were included in this study. Information was obtained about drug use, medical history, and demographics. The Mortality of stroke patients was observed for six months post-admission through direct or indirect communication. Statistical analyses included chi-square and t-tests, with a significance threshold set at $P < 0.05$.

Results: Increased mortality was correlated with advanced age (≥65 years), abdominal obesity, and the coexistence of diabetes and hypertension ($P < 0.05$). Poor outcomes of participants were also correlated with elevated inflammatory markers (ESR ≥40 mm/hr, CRP positivity, and IL-6 elevation). Interestingly, none of the corticosteroid-treated patients passed away ($P = 0.002$), indicating a possible protective effect of corticosteroids among stroke patients. There was no statistically significant correlation between NSAID use and survival. Conclusion: Older age, abdominal obesity, chronic (diabetes and hypertension), and elevated inflammatory markers are significant predictors of post-stroke mortality within six months. Corticosteroid use may be associated with improved survival, likely due to its anti-inflammatory effects, warranting further investigation.

Keywords: Ischemic stroke, Mortality predictors, Inflammatory markers

1. INTRODUCTION

Stroke is one of the health problems in the world. Stroke still causes deaths and long-term impairment. Stroke is one of the global health problems that contributes to death and long-term disability, leading to major health problems. (1) A stroke is a syndrome of interference with cerebral blood flow, which is either caused by a hemorrhagic or ischemic blockage, leading to neuronal damage and disrupting neuronal function. (2)

A large number of stroke patients show increased mortality within a few months of stroke onset, despite stroke management. Identifying mortality predictors within the first six months after stroke is essential to provide early care, optimize treatment plans, and improve outcomes.(3)

many factors can be used as predictors of mortality in patients with stroke, including age, sex, and a lower Glasgow Coma Scale (GCS) score. Besides the history of hypertension, heart problems, whether ischemic heart disease or congestive heart failure, or carotid stenosis, which contributed to higher rates of mortality among stroke patients.(4) Furthermore, the association of obesity with mortality in patients with stroke remains controversial.(5) Different risk factors, such as obesity, play a significant role in its prevalence and outcomes. Numerous studies concentrated on the association between body mass index (BMI) and stroke-related mortality, indicating that higher abdominal obesity is at an increased risk of stroke even at a normal BMI. Abdominal obesity is considered one of the leading causes of stroke, regardless of total body weight, taking into consideration the importance of measuring waist circumference and BMI.(6). The "obesity paradox," in some studies, shows that people who are overweight or obese have better post-stroke survival results than people who are normal or underweight. There may be an obesity paradox in stroke because numerous studies show that obese stroke patients have better results and lower mortality than individuals of normal body weight.(7). Variations in stroke subtypes, improved nutritional condition, or large metabolic reserves could all contribute to this event.(8)

Among hospitalized stroke patients, mortality has been attributed to complications such as aspiration pneumonia, sepsis, brain herniation, cardiorespiratory failure, cardiac arrest, heart failure, and multiorgan dysfunction.(9)

Inflammatory markers, including C-reactive protein (CRP), interleukin-6 (IL-6), tumor necrosis factor-alpha (TNF-α), the erythrocyte sedimentation rate (ESR), and fibrinogen, are elevated after acute stroke. Following an acute stroke, levels of inflammatory indicators—including C-reactive protein (CRP), interleukin-6 (IL-6), tumor necrosis factor-α (TNF-α), erythrocyte sedimentation rate (ESR), and fibrinogen—are commonly increased. (10)
Research indicates that higher levels of these biomarkers are linked to increased mortality, a greater risk of recurrent vascular events, and unfavorable functional outcomes.(11)
Elevated ESR reflects underlying inflammatory processes that contribute to atherosclerosis, thrombosis, and endothelial dysfunction, all of which play key roles in ischemic stroke pathogenesis. high ESR levels are associated with higher mortality. This test is easy to do, economical, and readily available, and it is a helpful parameter for monitoring disease activity.(12)

2. PATIENTS AND METHODS

This prospective cohort study was performed in a neurology ward of Basra Teaching Hospital, a tertiary care center in Basra City, southern Iraq. The study spanned six consecutive months, from February 1 to June 1, 2024. Patients who died before evaluation had a revised diagnosis inconsistent with stroke, were diagnosed with a transient ischemic attack, or had intracranial hematomas were excluded. 120 patients aged 18 years and above with ischemic stroke enrolled in this study. The primary outcome was stroke case fatality within six months. Patients were followed from hospital admission until the end of the study period. Mortality was assessed through close follow-up via weekly telephone interviews with the patients, their caregivers, or family members after hospital discharge. Since many patients passed away at home or in other healthcare facilities, death confirmation relied on the information provided by family members or caregivers.
We applied a pilot study to five percent of the participants. We measured the accuracy of the tools that were examined before we started the study. The results showed that the variable needed to be changed, so we changed the variable before we began data collection. We collected the data from the records and from in-person interviews with the patients or the caregivers. The first neurological assessments for all participants were done 24 hours after admission. I worked with the treating physicians. We performed laboratory testing, imaging studies, and clinical evaluations. We measured information, clinical history, lab results, therapy interventions, length of survival, and overall patient outcomes. Ethical approval from the Committee on Publication Ethics at the College of Medicine, University of Basrah was obtained before initiation of study. The study told each enrolled patient about the study goals. The study obtained written informed consent from each patient before the patient joined the study. Data were analyzed using the Statistical Package for the Social Sciences (SPSS), version 26, which was employed for data management and statistical evaluation. The information was expressed as percentages and frequencies. The variables were shown as mean ± standard deviation (SD). We used the chi-square test to evaluate correlations between variables. The chi-square test helped us see if the categories were related. We used the Shapiro-Wilk test to check normally distributed data. The Shapiro-Wilk test gave us a sense of normality. We used a two-sample t-test to compare the means of the two groups. The independent two-sample t-test showed whether the groups differed. For every analysis, a P-value of less than 0.05 was deemed statistically significant.

3. RESULTS:

The study findings show a link between age and survival outcomes. I see that the age group 65 to 85 years had a mortality rate of 28.3 percent while the age group 45 to less than 65 years had a mortality rate of 13.4 percent. The P value of 0.043 indicates that the age difference is statistically important. The sex factor did not show a link, with mortality; the P value was 0.582. Abdominal obesity was strongly linked to mortality ($P < 0.001$), as 52% of obese patients died, compared to only 11.6% of non-obese patients. Additionally, the presence of both diabetes and hypertension was significantly associated with mortality ($P < 0.001$), with 57.1% of patients with both conditions dying. In contrast, mortality was much lower in patients with only diabetes (9.3%) or hypertension (8.2%).

Table 3.1: Demographic characteristics

Variable		Survived cases (96)	Died cases after 6 months (24)	Total	P-Value*
Age	**45 to <65**	58 (86.6%)	9 (13.4%)	67	0.043
	65 to 85	38 (71.7%)	15 (28.3%)	53	
Sex	**Male**	54 (81.8%)	12 (18.2%)	66	0.582
	Female	42 (77.8%)	12 (22.2%)	54	
Abdominal Obesity	**Absent**	84 (88.4%)	11(11.6%)	95	<0.001
	Present	12(48%)	13(52%)	25	
Medical Disease	**DM**	39 (90.7%)	4 (9.3%)	43	<0.001
	HT	45 (91.8%)	4 (8.2%)	49	
	Both	12(42.9%)	16(57.1%)	28	

*Chi-Squire

Steroid use was highly protective, as none of the patients who used steroids died ($P = 0.002$), while 26.7% of those who did not use steroids died. However, the use of NSAIDs did not significantly influence survival ($P = 0.216$), though the mortality rate was slightly lower among NSAID users (14.0% vs. 23.4% in non-users).

Table 3.2: Drug history among the enrolled patients

Variable		Survived cases (96)	Died cases after 6 months (24)	Total	P-Value*
Steroids	**Not used**	66 (73.3%)	24(26.7%)	90	0.002
	Used	30(100.0%)	0 (0%)	30	
NSAIDs	**Not used**	59 (76.6%)	18 (23.4%)	77	0.216
	Used	37 (86.0%)	6 (14.0%)	43	

*Chi-Squire

Elevated inflammatory markers were strongly associated with mortality. Patients with an ESR ≥40 had a 50% mortality rate, compared to only 9.1% in those with ESR <40 ($P < 0.001$). Similarly, CRP positivity was significantly associated with higher mortality (45.8%) compared to CRP-negative patients (2.8%) ($P < 0.001$). Elevated IL-6 at discharge was also a major risk factor, with mortality reaching 39.7% among IL-6-positive patients, whereas only 1.6% of IL-6-negative patients died ($P < 0.001$). Furthermore, a history of inflammatory conditions significantly increased mortality (61.5% vs. 8.5%, $P < 0.001$), highlighting the role of chronic inflammation in poor outcomes.

Table 3.3: Inflammatory markers among the enrolled patients

Variable		Survived cases (96)	Died cases after 6 months (24)		P-Value*
ESR	**<40**	80 (90.9%)	8 (9.1%)	88	<0.001
	>=40	16 (50.0%)	16 (50.0%)	32	
CRP	**Negative**	70 (97.2%)	2 (2.8%)	72	<0.001
	Positive	26 (54.2%)	22 (45.8%)	48	
IL 6 at discharge	**Negative**	61 (98.4%)	1 (1.6%)	62	<0.001
	Positive	35 (60.3%)	23 (39.7%)	58	
History of inflammatory condition	**Absent**	86 (91.5%)	8 (8.5%)	94	<0.001
	Present	10 (38.5%)	16 (61.5%)	26	

*Chi-Squire

DISCUSSION

The current study shows that higher age has been described as the leading cause for mortality in patients with stroke; advanced age results in central nervous system damage, pre-existing vascular impairment, and diminished brain elasticity (13)

Elderly healthy individuals are associated with numerous noticeable changes in human intracranial and extracranial cerebral arteries.(14) notably brain herniation, multiple organ failure, dyslipidemia, community-acquired pneumonia, hypoproteinemia, and a history of hypertension, which is regarded as a prevalent problem associated with the aging process. All the preceding factors carry the risk of mortality among patients with stroke (9)

Historically, obesity has been recognized as a significant risk factor in the development of cardiovascular diseases, particularly stroke.(15). Abdominal obesity was associated with an elevated risk of major cardiovascular outcomes(16) . It is an independent, potent risk factor for ischemic stroke in all race-ethnic groups. (17)

Abdominal obesity accelerates atherosclerosis, which results in reduced blood supply to the brain, worsens stroke outcomes, and increases the likelihood of severe disability or death.(18)

This contributes to increased risk of hypertension, diabetes, and atrial fibrillation, increasing the risk of large artery and cardioembolic strokes, and risk of Larger strokes and higher mortality risk.(1)

Both diabetes and hypertension are well-established risk factors for stroke that substantially elevate mortality by promoting vascular and cerebrovascular damage. Chronic hypertension induces arterial wall degeneration, accelerating atherosclerosis and increasing susceptibility to severe ischemic stroke Moreover, uncontrolled hypertension heightens the likelihood of recurrent strokes, which carry an even greater fatality risk (19)

Plasma C-reactive protein (CRP) is one of the inflammatory markers, a key inflammatory biomarker, that has been consistently associated with an increased risk of stroke, particularly ischemic stroke. CRP, produced by the liver in response to interleukin-6 (IL-6), reflects systemic inflammation, which plays a crucial role in atherosclerosis, endothelial dysfunction, and thrombogenesis—key mechanisms underlying stroke pathogenesis. The current study found that elevated inflammatory markers IL6 and CRP were significantly correlated with increased mortality. Although interleukin-6 (IL-6) is primarily recognized for its proinflammatory functions, emerging evidence suggests a dual role in cerebral ischemia: (1) acting as an inflammatory mediator in the acute phase, and (2) assuming a neurotrophic role during the subacute to chronic phases, potentially contributing to neurorepair processes.(20)

Regarding CRP, Elevated levels were linked to a higher likelihood of recurrent stroke, composite vascular complications, and unfavorable functional outcomes. This marker may contribute to cerebral injury by accelerating atherosclerotic processes, triggering complement activation, suppressing fibrinolysis, and enhancing thrombus formation. Consequently, increased CRP concentrations may indicate more extensive cerebral tissue damage. (21)

High serum CRP level on admission may be helpful to assess severity and early outcome in ischemic stroke(22)

In this study regarding patients, those who used steroids had a significantly lower mortality rate compared to those who did not. The explanation for this is that stroke is associated with inflammation that exacerbates brain injury. Steroids are potent anti-inflammatory agents and may reduce secondary damage by suppressing harmful immune responses in addition to reducing brain edema and its role as immunomodulators.(23)

CRP, we still do not know the impact of inflammatory drugs (NSAIDs) on stroke mortality. My findings match studies that show the use of NSAIDs does not meaningfully improve survival for stroke patients. The lack of mortality benefit could be because NSAIDs mainly block cyclooxygenase (COX), which stops prostaglandin production and reduces inflammation and pain. (24) The study has limitations. The study took place at one tertiary care center. The single center could limit how well the study findings apply to groups. The study is observational. The observational study limits the ability to find relationships. The observational design limits the ability to see the effect of steroid use on survival. The study measured markers only while patients were in the hospital. The study's limited measurement of markers may not show how inflammatory markers change over time or reveal the ability of inflammatory markers to predict outcomes. I think the study shows that we need to identify high-risk stroke patients using both non-modifiable factors. Abdominal obesity and inflammatory biomarkers such as CRP and IL-6 may serve as valuable indicators of prognosis. The observed potential benefit of corticosteroids points toward new therapeutic avenues for reducing post-stroke mortality. Timely interventions targeting these factors may enhance patient outcomes in resource-limited settings

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