



ADMISSION C-REACTIVE PROTEIN AS A PROGNOSTIC BIOMARKER IN ACUTE ISCHEMIC STROKE: A PROSPECTIVE OBSERVATIONAL STUDY

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Abstract

Background:

C-reactive protein (CRP) is a sensitive biomarker of systemic inflammation. Elevated CRP has been implicated in vascular endothelial dysfunction, metabolic derangement, and atherothrombotic disease. Its prognostic significance in acute ischemic stroke (AIS) remains an area of clinical relevance. Despite the known associations between CRP levels and cerebrovascular outcomes, AIS remains underexplored in South Indian populations, where metabolic comorbidities are highly prevalent.

Objectives:

To evaluate the association between admission CRP levels and clinical outcomes in AIS and to examine correlations between CRP, blood pressure, and blood glucose.

Methods:

A prospective observational study was conducted on 100 radiologically confirmed AIS patients at Government Thiruvapur Medical College. Admission CRP, systolic and diastolic blood pressure (SBP, DBP), and blood glucose were recorded. Correlations were analyzed using Pearson's test, with $p < 0.05$ considered statistically significant.

Results:

Mean CRP was 18.12 ± 17.79 mg/L, SBP 146.40 ± 38.07 mmHg, DBP 89.50 ± 18.27 mmHg, and glucose 229.88 ± 122.78 mg/dL. Elevated CRP (>6 mg/L) was observed in 89% of patients. CRP correlated negatively with SBP ($r = -0.214$, $p = 0.032$) and DBP ($r = -0.261$, $p = 0.009$), while correlation with glucose was weak and non-significant ($r = 0.044$, $p = 0.662$). Patients with CRP >10 mg/L had a 41.6% mortality rate versus 9.1% in those with normal CRP levels.

Conclusion:

Elevated admission CRP is significantly associated with poor outcomes in AIS. Its significant inverse correlation with blood pressure suggests a hemodynamic–inflammatory interplay that may reflect vascular dysregulation in severe strokes. Integrating CRP testing into early stroke assessment could improve prognostication and guide anti-inflammatory or hemodynamic-targeted therapies.

Keywords: Acute ischemic stroke, C-reactive protein, inflammation, blood pressure, hyperglycemia, prognosis.

Introduction

Acute ischemic stroke (AIS) is a leading cause of mortality and long-term disability worldwide. Stroke remains one of the major contributors to global morbidity and mortality, accounting for nearly 11% of all deaths and representing a significant public health burden ^(1,2). Among all stroke subtypes, AIS constitutes approximately 85% of cases, resulting from the abrupt occlusion of a cerebral artery and the consequent interruption of blood flow to brain tissue ^(3,4). Despite advances in neuroimaging and reperfusion therapies, the prognosis of ischemic stroke continues to depend not only on the extent of vascular obstruction but also on the host's inflammatory response and metabolic status at presentation.

Beyond vascular occlusion, stroke represents a neuroinflammatory emergency characterized by cytokine release, oxidative stress, and endothelial dysfunction ^(5,6). Cerebral ischemia initiates a cascade of inflammatory and immunologic events, leading to endothelial activation, leukocyte infiltration, and the release of pro-inflammatory cytokines such as interleukin-6 (IL-6) and tumor necrosis factor-alpha (TNF- α) ^(5,6,7). These mediators stimulate hepatic synthesis of C-reactive protein (CRP), a sensitive acute-phase reactant that mirrors the intensity of systemic inflammation.

Among inflammatory biomarkers, CRP stands out because of its clinical accessibility, reproducibility, and strong association with cerebrovascular outcomes ⁽⁷⁾. CRP is a pentraxin family protein produced by hepatocytes in response to IL-6 and TNF- α stimulation. Plasma CRP levels may increase up to a thousandfold during acute inflammation, reflecting the magnitude of systemic immune activation ⁽⁸⁾. Elevated CRP has been associated with endothelial injury, atherosclerotic plaque instability, and microvascular thrombosis—mechanisms that critically shape the evolution of ischemic brain injury. Thus, elevated CRP levels are not merely byproducts but indicators of ongoing inflammatory injury within cerebral and vascular tissues ^(8,9,10).

A growing body of evidence suggests that CRP functions as both a biomarker and a mediator of vascular pathology. It can bind to damaged endothelial cells, activate the complement system, and promote the expression of adhesion molecules such as ICAM-1 and VCAM-1, thereby amplifying vascular inflammation ⁽¹⁰⁾. High-sensitivity CRP (hs-CRP) has been shown to predict stroke occurrence, infarct volume, and functional outcome, independent of traditional risk factors like hypertension, diabetes mellitus, and dyslipidemia ⁽¹¹⁾.

Hypertension and hyperglycemia, both frequent comorbidities among stroke patients, share inflammatory underpinnings. High CRP levels have been reported in both hypertensive and diabetic populations ^(11,12). Moreover, these comorbid states may potentiate the inflammatory response: elevated blood pressure contributes to endothelial dysfunction and shear stress, while acute hyperglycemia induces oxidative injury—both processes that enhance CRP synthesis and exacerbate ischemic damage ^(13,14,15). The interplay between vascular risk factors and systemic inflammation underscores the need to evaluate CRP as a unifying marker of disease activity and prognosis.

However, the precise relationship among CRP, blood pressure, and glycemia during the acute phase of ischemic stroke remains inadequately defined, particularly within the South Indian population. While CRP has been widely studied globally, data from South Indian populations are scarce, especially regarding its relationship with hemodynamic and glycemic parameters during AIS.

Aim of the Study

This study aims to determine the correlation between admission CRP levels, blood pressure, and blood glucose in patients with AIS, and to evaluate whether CRP can serve as a prognostic biomarker for disease severity and clinical outcome.

Methodology

This study was designed as a prospective observational study conducted in the Department of Medicine, Thiruvavur Medical College, Tamil Nadu, India. The study period extended from May 2021 to May 2022. Ethical clearance was obtained from the Institutional Ethics Committee, and all participants or their legally authorized representatives provided written informed consent prior to inclusion.

A total of 100 consecutive patients admitted with clinically and radiologically confirmed acute ischemic stroke (AIS) were enrolled in the study. Diagnosis was established based on clinical evaluation and CT or MRI brain findings showing evidence of cerebral infarction consistent with the presentation.

Inclusion Criteria

1. Patients aged ≥ 12 years of either sex.
2. Diagnosed cases of acute ischemic stroke confirmed by imaging.
3. Presentation within 72 hours of symptom onset.
4. Willingness to participate and provide informed consent.

Exclusion Criteria

1. Patients with hemorrhagic stroke, transient ischemic attack, or space-occupying lesions.
2. Evidence of ongoing systemic infection, sepsis, autoimmune disease, or malignancy.
3. Recent (< 1 month) major surgery, myocardial infarction, or trauma.
4. Patients on anti-inflammatory drugs, steroids, or immunosuppressants prior to admission.
5. Unwilling or uncooperative patients.

Sample Size Calculation

The sample size was determined using the formula:

$$n = \frac{Z^2 \times p(1 - p)}{d^2}$$

where $Z = 1.96$ for 95% confidence, $p = 0.60$ (expected prevalence of elevated CRP in AIS from previous studies⁽⁸⁾, and $d = 0.1$ (precision level).

The minimum required sample size was 92, which was rounded to 100 to improve statistical power and accommodate potential exclusions.

After obtaining consent, each patient underwent detailed clinical evaluation and systemic examination on admission.

The following data were collected using a predesigned proforma:

1. Demographic Data

- Age, sex, occupation, and residence.

2. Clinical Parameters

- Blood pressure: Systolic and diastolic readings measured in the right arm using a mercury sphygmomanometer after 5 minutes of rest, recorded to the nearest 2 mmHg.
- Sensorium: Classified as conscious, drowsy, or unconscious at presentation.
- Outcome: Recorded as recovered or died at discharge.

3. Laboratory Investigations

- C-Reactive Protein (CRP): Quantitative estimation performed by nephelometric method using a high-sensitivity CRP assay kit (normal range: < 6 mg/L).
- Blood glucose: Measured using the glucose oxidase–peroxidase method on a fully automated analyzer.
- Other routine parameters (CBC, electrolytes, renal and liver function) were recorded as part of standard stroke care but not analyzed in this study.

4. Neuroimaging

All patients underwent CT or MRI brain within 24 hours of admission to confirm infarct territory and exclude hemorrhagic stroke.

Operational Definitions

- High CRP: CRP > 6 mg/L at admission.
- Hypertension: SBP $\geq$ 140 mmHg and/or DBP $\geq$ 90 mmHg on two consecutive readings.
- Hyperglycemia: Random blood glucose > 200 mg/dL.
- Poor outcome: Death during hospital stay or severe residual neurological deficit at discharge.

Statistical Analysis

All data were entered into Microsoft Excel and analyzed using IBM SPSS Statistics version 26.0

1. Descriptive statistics: Mean $\pm$ SD for continuous variables; frequency and percentage for categorical data.

2. Normality testing: Done using the Shapiro–Wilk test.

3. Comparative tests:

- *Mann–Whitney U test* for comparison of continuous variables.
- *Chi-square test* for categorical data.

4. Correlation:

- *Pearson's correlation coefficient (r)* used to assess associations between CRP, blood pressure, and glucose.

5. Statistical significance: A *p*-value < 0.05 was considered statistically significant.

Ethical approval was obtained from the Institutional Ethics Committee of Government Thiruvavur Medical College prior to commencement of the study.

Results

Demographic Profile

A total of 100 patients diagnosed with acute ischemic stroke were included in the study. Of these, 60 (60%) were males and 40 (40%) were females, confirming a male predominance in ischemic stroke occurrence.

Physiological and Biochemical Parameters

All measured physiological and biochemical parameters were found to be elevated in the study group. The mean systolic and diastolic blood pressures were 146.4 mmHg and 89.5 mmHg, respectively, both significantly higher than standard reference values (*p* < 0.05). The mean blood glucose level was 229.9 mg/dL, indicating marked hyperglycemia, while the mean C-reactive protein (CRP) concentration was 18.12 mg/L, reflecting an elevated inflammatory state. The 95% confidence intervals were narrow, suggesting precise estimates of the true population means. (Table 1)

Table 1

Parameter	Mean Difference	95% CI (Lower–Upper)
Systolic BP (mmHg)	146.4	138.85–153.95
Diastolic BP (mmHg)	89.5	85.87–93.13
Blood Sugar (mg/dL)	229.9	205.52–258.71
CRP (mg/L)	18.12	14.59–21.65

Frequency of the Blood Pressure, Blood Sugar And C-Reactive Protein of Study Participants (Table 2)

Parameter	Variables	Frequency
Systolic Blood Pressure	Normal	11
	High	62
	Low	27
Diastolic Blood Pressure	Normal	15
	High	59
	Low	26

Blood Sugar	Normal	5
	High	69
	Low	26
C-Reactive Protein	Normal	11
	High	89

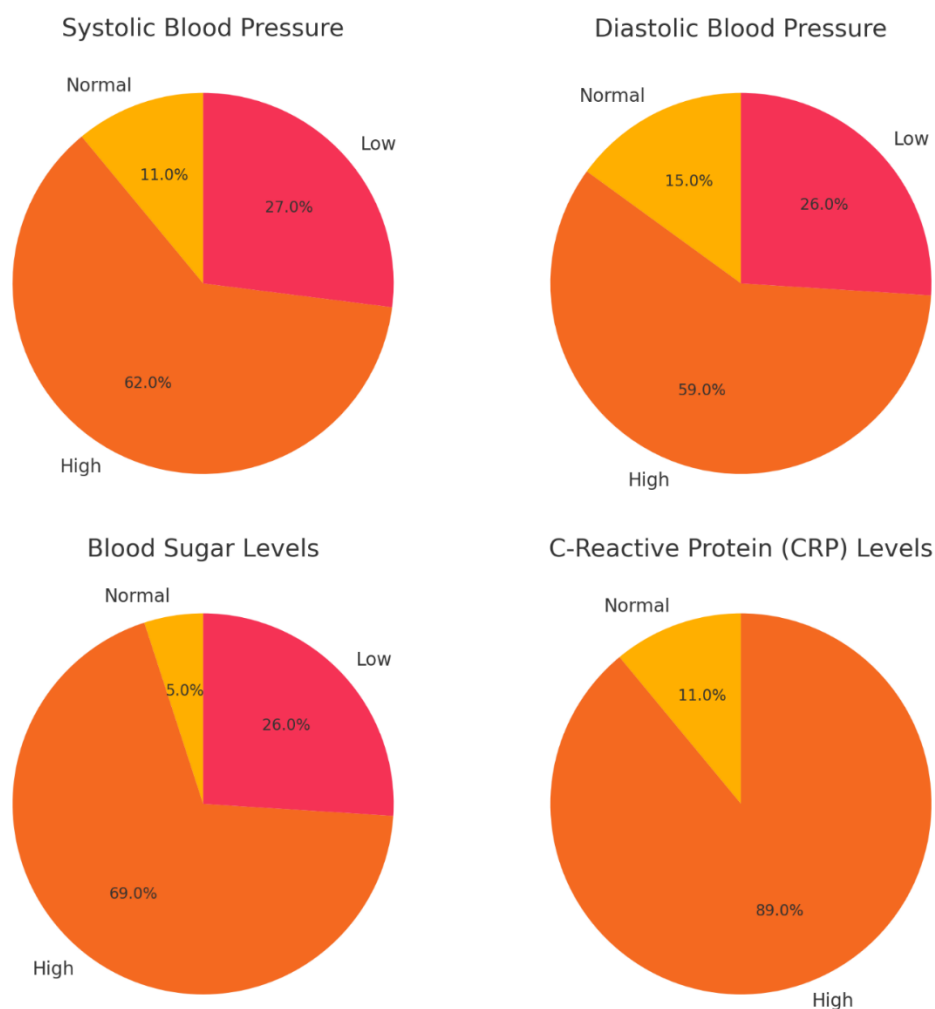
Table 2 shows Elevated C-reactive protein (CRP) levels (>6 mg/L) were found in 89% of participants, signifying a prominent inflammatory response. Only 11% exhibited normal CRP values, underscoring the inflammatory nature of acute ischemic pathology.

Systolic blood pressure was elevated in 62% and diastolic pressure in 59% of patients, reflecting a strong correlation between hypertension and ischemic vascular events.

Furthermore, blood glucose was elevated in 69% of the cohort, while 26% presented with hypoglycemia — indicating significant metabolic dysregulation during ischemic episodes.

Figure 1

Distribution of Blood Pressure, Blood Sugar, and CRP Among Study Participants



Correlation Analysis

Correlation coefficients were computed to explore associations between CRP, blood pressure, and blood glucose (Table 3).

A negative correlation was found between CRP and both SBP ($r = -0.214$, $p = 0.032$) and DBP ($r = -0.261$, $p = 0.009$), both statistically significant.

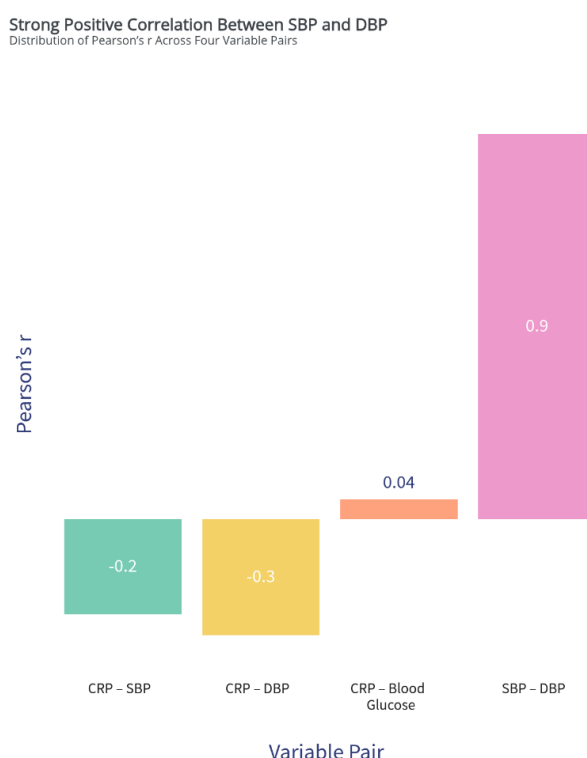
In contrast, the correlation between CRP and blood glucose was weakly positive but not significant ($r = 0.044$, $p = 0.662$).

A strong positive correlation was seen between SBP and DBP ($r = 0.868$, $p < 0.001$), confirming hemodynamic interdependence.

Table 3. Correlation between C-reactive protein (CRP), blood pressure, and blood glucose

Variable Pair	Pearson's r	p-value	Significance	Interpretation
CRP – SBP	–0.214	0.032	Significant	Higher CRP associated with lower systolic BP
CRP – DBP	–0.261	0.009	Significant	Higher CRP associated with lower diastolic BP
CRP – Blood Glucose	+0.044	0.662	not significant	No meaningful correlation with glucose levels
SBP – DBP	+0.868	<0.001	Highly Significant	Strong hemodynamic interdependence

CRP = C-reactive protein; SBP = systolic blood pressure; DBP = diastolic blood pressure;
Figure 2



Correlation coefficients were computed to explore the associations between admission C-reactive protein (CRP), blood pressure parameters, and blood glucose. (Figure 2)

A statistically significant negative correlation was observed between CRP and both systolic blood pressure (SBP) ($r = -0.214$, $p = 0.032$) and diastolic blood pressure (DBP) ($r = -0.261$, $p = 0.009$), indicating that higher levels of systemic inflammation were associated with lower blood pressure values.

The relationship between CRP and blood glucose was weakly positive but not statistically significant ($r = 0.044$, $p = 0.662$).

As expected, a strong positive correlation existed between SBP and DBP ($r = 0.868$, $p < 0.001$), reflecting normal hemodynamic coupling between the two parameters.

These findings suggest that in patients with acute ischemic stroke, elevated inflammatory response (higher CRP) may accompany a relative reduction in blood pressure, possibly due to systemic inflammatory vasodilation or altered cerebral autoregulation.

However, CRP did not demonstrate any significant correlation with blood glucose, implying that the inflammatory state at admission may not be directly linked to metabolic stress or glycemic status in this cohort.

Outcome Correlation

Patients with elevated CRP (>6 mg/L) demonstrated a markedly poorer prognosis. Mortality among this group was 41.6%, compared to 9.1% among patients with normal CRP levels. This suggests that raised CRP at admission is associated with adverse clinical outcomes and may serve as an independent prognostic indicator.

All continuous variables (SBP, DBP, blood glucose, and CRP) followed a non-normal distribution and were analyzed using non-parametric tests. The correlation results remained consistent across statistical methods, confirming the reliability of findings. A significance level of $p < 0.05$ was accepted for all analyses.

This study establishes a strong link between elevated admission CRP and adverse outcomes in acute ischemic stroke. The high prevalence of elevated CRP among stroke patients supports its role as a biomarker of neuroinflammation and a potential prognostic marker for mortality and functional recovery.

Discussion

The present study evaluated the prognostic significance of admission C-reactive protein (CRP) in patients with acute ischemic stroke (AIS) and its correlation with blood pressure and glycemic indices. Nearly 90% of participants exhibited raised CRP levels, confirming that systemic inflammation is a near-universal feature of acute cerebral ischemia. A notable inverse correlation between CRP and both systolic and diastolic blood pressure further suggests that heightened inflammatory response may coexist with hemodynamic instability in severe stroke.

CRP as an Indicator of Systemic Inflammation in Stroke

C-reactive protein, a hepatic acute-phase reactant induced by interleukin-6 (IL-6) and tumor necrosis factor-alpha (TNF- α), serves as a sensitive marker of systemic inflammation following ischemic insult. In this study, the mean CRP value at admission was 18.12 ± 17.79 mg/L, with 89% of patients showing elevated levels. This observation mirrors earlier findings that ischemic stroke triggers a robust inflammatory response, reflected by elevated circulating CRP concentrations⁽⁸⁾.

Hertog et al. reported that CRP levels ≥ 7 mg/L within 12 hours of symptom onset independently predicted mortality and poor outcome at three months, a finding consistent with our results.⁽¹²⁾ Similarly, Di Napoli et al. demonstrated that early CRP elevation correlated with infarct volume and neurological deterioration. These data collectively confirm that early CRP rise in AIS represents not only a marker of inflammation but also a surrogate for infarct severity and tissue damage.⁽¹⁰⁾

Hemodynamic Correlates and CRP Dynamics

A statistically significant negative correlation was found between CRP and systolic ($r = -0.214$, $p = 0.032$) and diastolic ($r = -0.261$, $p = 0.009$) blood pressures. Although hypertension is typically associated with increased inflammatory activity, this inverse relationship may reflect acute hemodynamic instability in the early phase of stroke. Elevated CRP levels may indicate impaired cerebral autoregulation and vascular endothelial dysfunction rather than systemic hypotension.

Experimental studies have shown that angiotensin II stimulates vascular smooth muscle cells to produce IL-6, monocyte chemoattractant protein-1 (MCP-1), and soluble intercellular adhesion molecule-1 (sICAM-1), which promote endothelial inflammation and microvascular thrombosis⁽⁸⁾. These cytokine-mediated processes exacerbate ischemic injury and contribute to poor outcomes. The observed inverse correlation between CRP and blood pressure may thus represent a compensatory physiological mechanism wherein inflammation-induced endothelial dysfunction limits autoregulatory vasoconstriction.

CRP and Glycemic Dysregulation

The weak positive but non-significant correlation between CRP and blood glucose ($r = 0.044$, $p = 0.662$) observed in this study supports the notion that hyperglycemia potentiates inflammation but does not always show a linear correlation with inflammatory biomarkers in smaller cohorts. Cai et al. reported that variability in blood glucose levels in AIS patients receiving thrombolytic therapy correlated with elevations in IL-6, MMP-9, TNF- α , and hs-CRP, and predicted poorer functional recovery. This supports the hypothesis that metabolic stress and inflammatory activation act synergistically to worsen ischemic injury.⁽¹³⁾

CRP and Clinical Outcome

In the present study, mortality was five times higher among patients with elevated CRP (>10 mg/L) compared to those with normal CRP levels. This finding aligns with the observations of Pfutzner et al., who demonstrated that hs-CRP independently predicted adverse cardiovascular outcomes even after adjusting for traditional risk factors such as diabetes and hypertension.⁽¹⁴⁾ Elevated CRP promotes tissue factor expression, low-density lipoprotein oxidation, and atheromatous plaque instability, suggesting that it not only serves as a marker but also plays a causal role in ischemic pathophysiology.^(8,11)

Comparison with Previous Studies

Our findings corroborate those of Chen et al., who established a positive longitudinal association between CRP and hypertension in Chinese adults, and of Suganya et al., who reported a combined impact of obesity, hypertension, and elevated CRP on the development of type 2 diabetes. Together, these studies support the concept that CRP lies at the intersection of metabolic and vascular inflammation, serving as an integrative biomarker of cardiovascular risk across diverse populations.^(11,12)

The Inflammation–Vascular–Metabolic Triad

The results of this study underscore the intricate interplay among systemic inflammation, hypertension, and hyperglycemia in driving ischemic brain injury. Elevated CRP likely represents the biological convergence of these risk factors—marking endothelial injury, oxidative stress, and cytokine-mediated neuronal death. The observed mortality gradient across CRP strata further highlights its prognostic value in predicting short-term outcomes in AIS.^(8,13)

Clinical Implications

From a clinical perspective, admission CRP measurement offers a simple, cost-effective, and widely available biomarker to assess inflammatory activity and stratify risk in AIS. Given its significant association with mortality, integrating CRP assessment into early management protocols may help identify high-risk patients who could benefit from intensive monitoring, strict blood pressure and glycemic control, or targeted anti-inflammatory interventions.

Limitations

This study's limitations include its single-center design and modest sample size, which may limit generalizability. Moreover, CRP and hemodynamic parameters were measured only once at admission; serial measurements could provide greater insight into the dynamic relationship between inflammation and clinical progression. Future studies should include additional inflammatory mediators, such as IL-6 and TNF- α , to elucidate mechanistic pathways.

Conclusion

The present study establishes that elevated admission CRP levels are significantly associated with poor prognosis and increased mortality in acute ischemic stroke. The inverse correlation between CRP and blood pressure and its relationship with hyperglycemia underscore the complex interaction

between vascular, metabolic, and inflammatory mechanisms. Admission CRP, therefore, serves not only as a biomarker of inflammation but also as a powerful prognostic indicator, meriting routine evaluation in the acute management of ischemic stroke.

References

1. Lozano R, Naghavi M, Foreman K, et al. Global and regional mortality from 235 causes of death for 20 age groups in 1990 and 2010: a systematic analysis for the Global Burden of Disease Study 2010. *Lancet* 2012; 380:2095–128. [https://doi.org/10.1016/S0140-6736\(12\)61728-0](https://doi.org/10.1016/S0140-6736(12)61728-0); PMID: 23245604.
2. Feigin VL, Norrving B, Mensah GA. Global burden of stroke. *Circ Res* 2017;120:439–48. <https://doi.org/10.1161/CIRCRESAHA.116.308413>; PMID: 28154096.
3. Bejot Y, Bailly H, Durier J, Giroud M. Epidemiology of stroke in Europe and trends for the 21st century. *Presse Med* 2016;45:e391–8. <https://doi.org/10.1016/j.lpm.2016.10.003>;
4. Lavados PM, Hennis AJ, Fernandes JG, et al. Stroke epidemiology, prevention, and management strategies at a regional level: Latin America and the Caribbean. *Lancet Neurol* 2007;6:362–72. [https://doi.org/10.1016/S1474-4422\(07\)70003-0](https://doi.org/10.1016/S1474-4422(07)70003-0).
5. Pepys MG and Hirschfield GM. C-reactive protein: a critical update. *J Clin Invest* 2003;111(12).
6. Black S, Kushner I, Samols D. C-reactive protein. *J Biol Chem* 2004;279:48487–48490.
7. Chandrashekara S. C - reactive protein: An inflammatory marker with specific role in physiology, pathology, and diagnosis *IJRCI*. 2014;2(S1):SR3
8. Leonardi-Bee J, Bath PMW, Phillips SJ, Sandercock PAG; for the IST Collaborative Group. Blood Pressure and Clinical Outcomes in the International Stroke Trial. *Stroke*. 2002; 33: 1315–1320.
9. Robinson T, Waddington A, Ward-Close S, Taub N, Potter J. The predictive role of 24-hour compared to casual blood pressure levels on outcome following acute stroke. *Cerebrovasc Dis*. 1997; 7: 264–272.
10. Bath FJ, Bath PMW. What is the correct management of blood pressure in acute stroke? The Blood Pressure in Acute Stroke Collaboration. *Cerebrovasc Dis*. 1997; 7: 205–213.
11. Chen B, Cui Y, Lei M, Xu W, Yan Q, Zhang X, Qin M, Xu S. C-Reactive Protein Levels in relation to Incidence of Hypertension in Chinese Adults: Longitudinal Analyses from the China Health and Nutrition Survey. *International journal of hypertension*. 2021 Dec 10;2021.
12. Kanmani S, Kwon M, Shin MK, Kim MK. Association of C-reactive protein with risk of developing type 2 diabetes mellitus, and role of obesity and hypertension: a large population-based Korean cohort study. *Scientific reports*. 2019 Mar 14;9(1):1-8.
13. Cai Y, Zhang H, Li Q, Zhang P. Correlation Between Blood Glucose Variability and Early Therapeutic Effects After Intravenous Thrombolysis With Alteplase and Levels of Serum Inflammatory Factors in Patients With Acute Ischemic Stroke. *Frontiers in Neurology*. 2022 Feb 22;13:806013
14. Pfützner A, Schöndorf T, Hanefeld M, Forst T. High-sensitivity C-reactive protein predicts cardiovascular risk in diabetic and nondiabetic patients: effects of insulin-sensitizing treatment with pioglitazone. *Journal of diabetes science and technology*. 2010 May;4(3):706-16.
15. Ghule A, Kamble TK, Talwar D, Kumar S, Acharya S, Wanjari A, Gaidhane SA, Agrawal S. Association of Serum High Sensitivity C-Reactive Protein With Pre-diabetes in Rural Population: A Two-Year Cross-Sectional Study. *Cureus*. 2021 Oct 28;13(10).