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#### 4 The Association Between Pro-Inflammatory Cytokines and C-Reactive Protein and the Cognitive and Neurological Outcome in Stroke Survivors: A Systematic Review

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**Objective:** Childhood ischemic and hemorrhagic stroke is often associated with neuropsychological and cognitive deficits. Stroke induces an inflammatory response in the central and peripheral nervous systems. High levels of inflammatory markers in the plasma have been associated with poorer cognitive outcomes. The role of inflammation in neurological prognosis of stroke has been studied previously; however, there is a limited understanding of the association between inflammatory markers and neuropsychological outcome post-stroke. The present review examined the existing literature on the association between inflammatory markers and post-stroke functioning.

**Participants and Methods:** Data bases (PsycINFO, PubMed, Web of Science, and Ovid) were reviewed in October 2020. Articles were restricted to English-language literature. Articles were included regardless of recruitment setting, number of strokes, mechanism of stroke, timing of blood collection and outcome assessment. The articles focused on patients with stroke (between the ages of 0 to 95), measured post-stroke outcome by neurological and cognitive outcome measures (i.e., it included findings on any aspect of cognition such as memory, information processing, or attention), and on pro-inflammatory cytokines and c-reactive proteins as measures of inflammation. The systematic literature search retrieved 954 articles to review against inclusion criteria. Descriptive statistics were performed using IBM SPSS 27.0 Statistics Software.

**Results:** A total of 18 articles were included in this review. The population age ranged from 21 to 95, and, when reported (n=17), mean

participant age was 66.31. Among stroke patient populations, ischemic stroke was most researched (n=15). The most widely investigated biomarkers were CRP (n=9), IL-6 (n=8), TNF- $\alpha$  (n=7), IL-1 $\beta$  (n=5), and IL-10 (n=5). The time of initial blood collection ranged from on admission to within 3 months poststroke. Equal number of studies used both neurological and cognitive tests (n=7), or only neurological (n=7), 2 studies only used cognitive tests, and one study used all three types of measures. The most commonly used cognitive test was the Mini Mental State Examination, MMSE (n=7). The next commonly used cognitive test was the Montreal Cognitive Assessment (MoCA), (n=4). Only two studies used a comprehensive neuropsychological battery.

**Conclusions:** There is a lack of research into diverse stroke populations. All the studies examined the association between inflammatory markers and the post-stroke outcomes in adult populations and mostly in patients with ischemic stroke. The lack of research on pediatric and young adult stroke represents a significant gap in understanding predictors of neurological and cognitive outcomes. Further, the review revealed a lack of comprehensive neurocognitive assessment post stroke, with most studies measuring neuropsychological outcome using brief cognitive instruments. Our findings highlight a critical need for addressing the above gaps to help elucidate the role of inflammatory markers in the neuropsychological prognosis of stroke in younger populations.

**Categories:** Stroke/Cerebrovascular Injury & Disease (Child)

**Keyword 1:** stroke

**Keyword 2:** cognitive functioning

**Keyword 3:** neuroimmunology

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