



Chronic depression and post-chikungunya rheumatological diseases: Is the IL-8/CXCL8 another associated mediator?



Dear editor

We have read with interest the systematic review of van Aalst [1], about the long-term sequelae of chikungunya (CHIK) virus disease. In that regard, considering the significant number of cases that have been reported in the region of the Americas during the last 3 years (over 2 million) [2], especially in Colombia and Brazil, their findings are of concern. We agree on the fact that the quality of life is significantly affected in chronic chikungunya, not only as consequence of rheumatological sequelae, e.g. post-CHIK chronic inflammatory rheumatism (pCHIK-CIR), but also as the compromise of mental health [1], which can be affected by the occurrence of depression, anxiety, memory problems, ideational slowdown [3], and even sleep disorders [4].

Chikungunya immune response is a complex scenario in which, during acute as well chronic disease, multiple immunopathological mechanisms and mediators are involved [5]. Among them, multiple cytokines, such as IL-6 and TNF- α , which are also related to the development of depression and other mental disorders [1,4,5].

Depression is a complex and a heterogeneous disease, with several etiopathological hypotheses [5]. Beyond the classical theories of this disorder, such as: monoaminergic, hypothalamic–pituitary–adrenal axis (HPA axis), stress of the neuroendocrine system theories, other emerging concepts have been described. The inflammatory model of depression has been postulated since 1990.

There is evidence that depressive symptoms associated with chronic diseases, such as pain, fatigue, cachexia and sleep disorders, are strongly linked with inflammation and then cytokine expression [5].

Depression-inflammation relationship is bidirectional, in other words, the first increases certain immunobiomarkers, and in the

opposite way, cytokines influence depressogenic findings; additionally, both alterations would occur concurrently.

The molecular mechanisms by which cytokines may impact behavior are still largely unknown, but there are some theories with regard with neurotransmitters function, metabolism and modification of the neuroendocrine physiology, especially of the HPA axis [5].

In addition to IL-6 and TNF- α , other cytokine seems to be relevant for depression, but particularly specific forms, such as chronic, fatigue, cachexia and sleep disorders. This is the case of IL-8/CXCL8. This interleukin can be secreted in the brain by astrocytes and microglia, which is relevant in neuroimmune surveillance and neuroprotection. IL-8/CXCL8 would be elevated in chronic inflammatory diseases (e.g. pCHIK-CIR), depressive disorders, and in its comorbidity. Its levels are correlated with depression severity and persistence.

Finally and highlighting the importance of further studies of psychiatric disorders, particularly depression, in association with arboviral diseases, based on the available evidence, the summary of them should consider that IL-8/CXCL8 as well IL-6, TNF- α , IL-1 β and IL-12, are increased in different ways during acute and chronic chikungunya disease and also associated with specific symptoms, forms and characteristics of depression, such as chronic form, fatigue, pain, major depression in elder people, depression with atypical features, anxiety, and predominance in women (Table 1). All the above, adds hypotheses to the growing evidence and the need for research not just in the clinical interaction between arboviral and psychiatric disorders [1], but also at immunological detail [5]. This will provide the basis for potential interventions (e.g. immunomodulators) that may mitigate the impact of chikungunya and its long-term sequelae, which include mental and neurological compromise [1,2,5].

Table 1

Selected cytokines, growth factors, and chemokines during acute and chronic phases of chikungunya disease and their association with psychiatric disorders [1,4,5].

Cytokine	Chikungunya disease(cytokine levels)		Psychiatric disorders	
	Acute	Chronic	Predominant association	Cytokine Levels
IL-1 β	↑	↑↑↑	Major depression, especially in elder people	↑
TNF- α	↑	↑↑↑	Depression with atypical features	↑↑↑
IL-6	↑↑↑	↑	Depression and anxiety	↑↑↑
IL-8/CXCL8	↑↑↑	↑	Chronic depression, fatigue and pain	↑
IL-12	↑↑↑	↑	Depression in women	↑

↑ = Elevated; ↑↑↑ = Highly Elevated.

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Conflict of interest

None of the authors report conflict of interests.

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