

# Migraine in Children and its Relationship to Biomarkers



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## Introduction

Migraine is a clinical manifestation of severe, recurrent and most commonly disabling headache disorder in children and adolescents which is associated with nausea and sensitivity to light and sound. Primary headache disorders such as migraine begin as early as childhood or adolescence and the prevalence increases during primary school and adolescence [1]. It is very commonly encountered by neurologists. Bio-psycho-social factors play a vital role in migraine and sometimes it is triggered by factors. Triggers that induce migraine are stress [2], fatigue, various foods, alcohol, drugs, smoking, weather changes, and odors [3]. Migraine is diagnosed clinically.

## Pathogenesis

Migraine is a primary brain disorder with abnormalities in pain modulating systems and cortical stimulus processing. Migraine is thought to be a consequence of cortical hypersensitivity, cortical hyperactivity and lack of habituation. Migraine with aura has been specified as a risk factor for vascular disorder. Mast cells perivascular area linked to dura in neurons can be triggered by trigeminal nerve, sphenopalatine ganglion and neuropeptides which leads to secretion of vasoactive mediators thus contributing to pathogenesis of migraine. As far as genetic makeup is concerned, T/T genotype, MTHFR T/T homozygosity [4], TSPAN2 single nucleotide polymorphisms (SNPs) rs12134493 and rs2078371 are thought to be involved in pathogenesis of migraine. Familial Hemiplegic Migraine (FHM) subtype 3 is caused by mutations in SCN1A mutation [5].

## Association, Diagnosis and Treatment

Conditions thought to be comorbid with migraine includes asthma, anxiety, depression and other chronic pain conditions. ADHD, insomnia, allergic disease, obesity, Eidlitz, narcolepsy [6-10], cognitive defects, epilepsy, olfactory hallucination, cyclic vomiting syndrome, tumor of the hypothalamic-pituitary region, overdose of glucocorticoids or growth hormone and sickle cell disease are associated with migraine [11-16]. Migraine is diagnosed clinically but measurement of VEP visual evoked potential latency and amplitude is a reliable test for the diagnosis of migraine in children with vague symptoms [17]. Sometimes MRI of pediatric patients with migraine can show structural

changes such as grey matter atrophy of frontal and temporal lobes and increased volume of the right putamen. The left fusiform gyrus had an increased volume in patients with aura whereas it was significantly atrophied in patients without aura [18].

Avoiding triggers, providing cool and calm environment, analgesic and abortive therapies are usually used to treat migraine in children. CGRP monoclonal antibodies [19] are an innovative therapy for migraine. Stress management therapies have been reported to be effective in reducing headache related disabilities in teens. Hybrid cognitive-behavioral therapy is feasible option for youth with co-occurring chronic migraine and insomnia. Two mind-body techniques, transcendental meditation or hypnotherapy and progressive muscle relaxation exercises are equally effective in reducing primary headache in children [20].

## Biomarkers

Biomarkers are substances released in response to some particular phenomena taking place inside the organism. It is a partially discovered territory in field of medicine and has a lot to offer. Biomarkers are also playing a vital role in determining pathogenesis and diagnosis of migraine as well as in studying the treatment response of different migraine therapies. MicroRNAs (miRNAs) are small molecules which regulates immune and neuronal processes has been reported in patients with migraine and ischemic stroke. These MicroRNAs can be used as an indicator of precocity for clinical and/or pharmacological intervention of migraine [21]. Migraine is a clinical diagnosis it is very challenging to pick it in infants and juvenile population. MiR-590-5p which is a biomarker for general pain, can be used to diagnose the migraine and to biomarker of general pain and to evaluate the efficacy of the drug treatment [21]. Recurrent and severe headache in children and adolescents make them vulnerable to long term vascular morbidity and is associated with increase body mass index, C-reactive protein and homocysteine levels and decreased serum red blood cells and folate levels [22].

A direct relation between childhood migraine attacks and increased production of glial S100beta protein [23] has been established and it may be a useful biochemical marker for migraine in acute recurrent headache in childhood. Studies on biomarkers

have provided information regarding pathogenesis of migraine. Oxidative stresses effect native thiol levels in body. Native thiol levels are remarkably higher in patients suffering from migraine. This might support the notion that oxidative stress has a role in pathogenesis of migraine. Elevation in s100b levels occurs during migraine attack but the peak is detected in the pain-free period after 2-4 days. Neuron specific enolase levels decrease during migraine [24]. This supports the idea of disruption of blood brain barrier during and after migraine attack. Children with migraine present with the higher levels of anticardiolipin antibody [25-27] but the mean values were within the normal range. The role of anticardiolipin antibody in pathogenesis of migraine remains unclear.

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