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Short Communication

Migraine and Insulin Metabolism Linked with Glutamate Excitotoxicity-

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ABSTRACT

Migraine is a migrainous brain condition distinguished by a reduced threshold of neuronal hyper-excitability. There are two types of migraine: migraine with aura and migraine without aura. It is more prevalent in adult females (12%-17%) than males (4%-7%) and has a general prevalence rate ranging from 2.6 to 21.7 percent. Co-morbidities linked to migraine are diabetes, depression, ischemic strokes, hypertension, asthma, dementia, cardiovascular disorders, sleep disorders, etc. We are concerned about metabolic diseases such as diabetes since diabetic patients have higher glucose levels, which are also found to be greater in migraine sufferers. Glutamate is generated in response to high glucose levels in the brain, which subsequently activates TNF production, which can exacerbate excitotoxicity. TNF- has a role in neurogenic neuroinflammation, which plays a role in migraine pathophysiology. This brief communication piece shows that consuming a low glycemic index diet can be an effective and dependable strategy for reducing migraine attacks.

Keywords: Migraine; Insulin metabolism; Glutamate excitotoxicity

INTRODUCTION

Migraine has been around since Hippocrates' time (c.460-c.370 B.C.) and we've learned a lot about it since then. Migraine is a polygenic, dysautonomic, complicated neurological condition marked by a "lower threshold of neuronal hyper-excitability" known as "the migrainous brain" with vascular dysfunction as consequence and show distinctive periodicity [1]. ICHD-3 (International Criteria for Headache Disorder -3rd edition) has classified migraine into 2 main types including episodic migraine which is further classified into Migraine with Aura (MA), Migraine without Aura (MWA), and Chronic Migraine (≥ 14 migraine attacks/month) with the prevalence rate of 1-2% [2].

Migraine is a widespread and severe disorder with a higher incidence rate (Figures 1A & 1B) and affects 2.7 to 10.0% of early childhood. It affects both sexes equally but is more frequent in adult females (12% -17%) than males (4%-7%). It affects one out of every ten persons with prevalence rates ranging from 2.6 to 21.7 percent and an average variation of 12 percent between nations including India. It causes more disability and poses high Disability-Adjusted Life Years (DALYs) per 100,000,000 people worldwide [3-5].

Cardinal symptoms include Unilateral headache, vomiting, phonophobia, and photophobia are common symptoms, although some patients also report stomach and abdominal discomfort, dizziness, pale skin, weariness, and other symptoms. Different treatments have been developed, but no cure has yet been discovered, as all drugs are symptomatic [6].

Co-morbidities linked to migraine many such as depression, hypertension, asthma, ischemic strokes, hypertension, dementia, cardiovascular disorders, sleep disorders, and metabolic disorder like diabetes [7,8]. Patients with metabolic syndrome have a higher age, have a higher number of migraine stimuli, have a longer migraine attack duration, and have a longer migraine history [8].

HIGHER GLUCOSE AND MIGRAINE POSSIBLE LINK

Glucose and migraine have a long history and several studies indicate that migraine patients had higher plasma glucose levels [9]. Blood glucose levels in headache patients may be raised because migraineurs' insulin levels are disrupted [8,10]. Higher plasma glucose levels during spontaneous migraine attacks, independent of aura symptoms and unrelated to pain intensity, peaking in the early

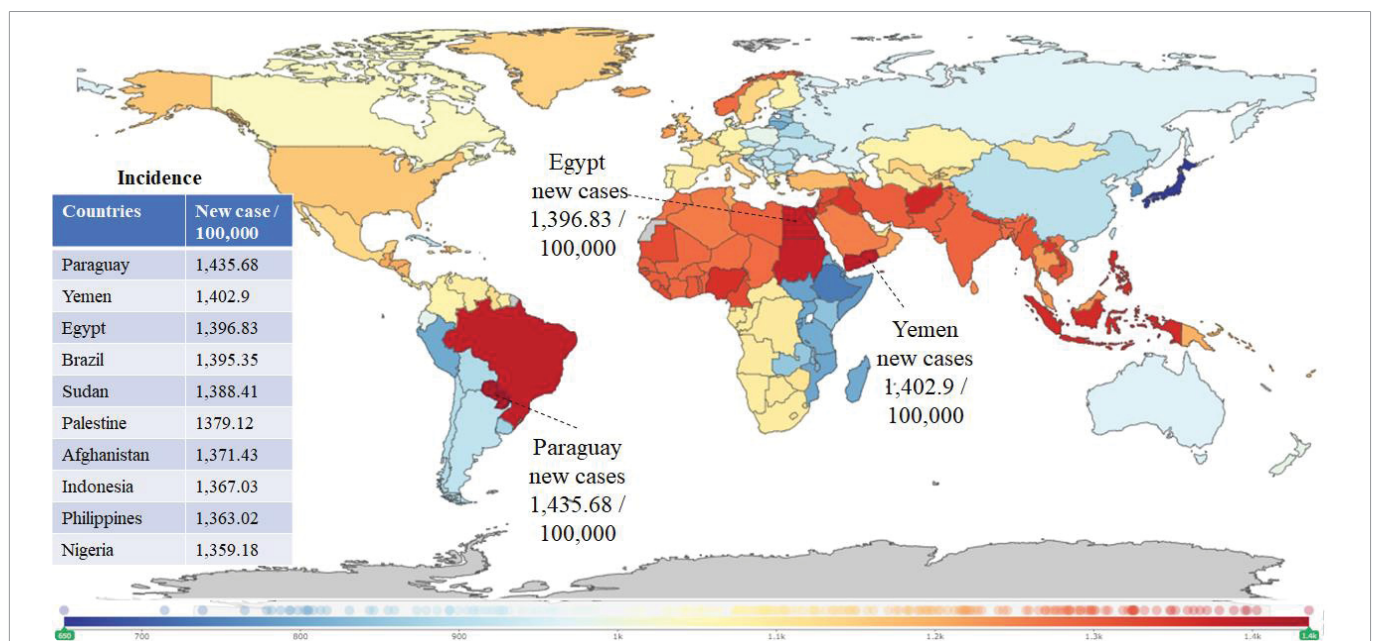


Figure 1a: (Global Burden of Diseases 2019): World's top 10 countries with highest incidence of migraine (both sex, 2019 Global Burden of Diseases of 2019 per 100,000) (<https://www.healthdata.org/data-visualization/gbd-compare>).

stages of attacks [9]. An impaired response of the body to insulin, resulting in elevated levels of glucose in the blood [11] and it is found that an altered IR status, particularly when it is in partnership with obesity [12]. In people with chronic migraine, insulin resistance may raise the chance of developing type 2 diabetes in the future [13]. It has also been established that insulin receptor SNP (single-nucleotide polymorphisms) are linked to migraine [14] which results in altered function of the protein.

High Glucose (HG) induced the various changes of energy-related metabolites, such as increased succinate and creatine phosphate also reduction in intracellular lactate, increased levels of intracellular alanine, phenylalanine, myoinositol, branched-chain amino acids (isoleucine and valine), and choline, and also decreases in intracellular dimethylamine, dimethylglycine, and 3-methylhistidine which may indicate downregulation of methyl group metabolism [15].

As it is found that due to HG there is increased production of glutamate from the branched-chain amino acids (isoleucine and valine) [15,16] and glutamate has a strong association with the condition [17]. Glutamate binds to the mGluR2 to induce TNF- α production and TNF- α can potentiate excitotoxicity (Figure 2) [18].

To enclose this, the patient should stick to a strict low-glycemic-index diet, which is an effective and dependable migraine-reduction strategy [19].

CONCLUSION

Migraine is a prevalent disorder that is characterized by reduced neuronal hyperexcitability and has two main types as MA and MWA. Migraine is linked to various disorders including metabolic disorders like diabetes characterized by high blood glucose (HG). Hyperglycemia

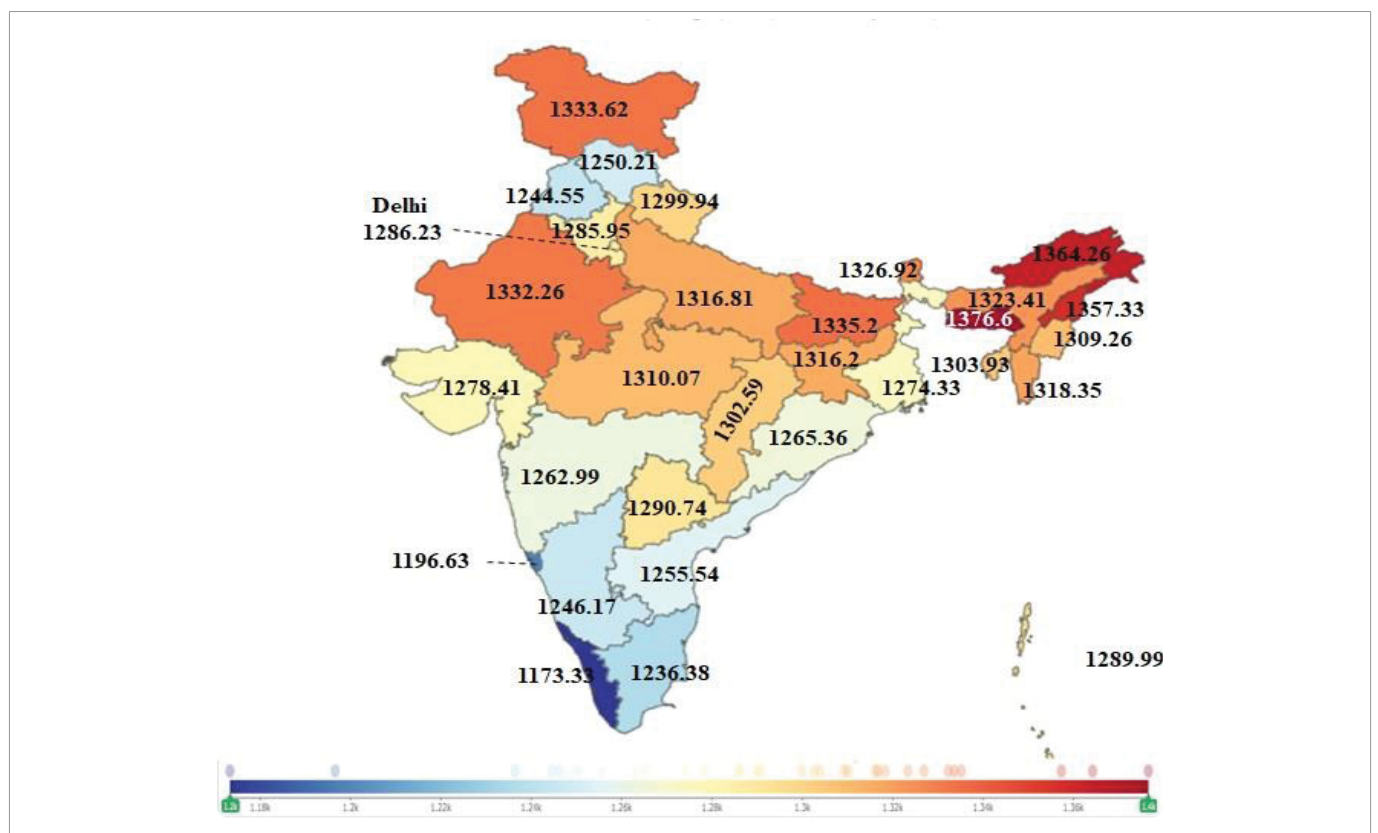


Figure 1b: (Global Burden of Diseases 2019): Incidence of migraine (adjusted for both sex, Global Burden of Diseases 2019 data per 100,000) with the 3 highest state with new cases found in Meghalaya, Arunachal Pradesh, and Nagaland (<https://www.healthdata.org/data-visualization/gbd-compare>).

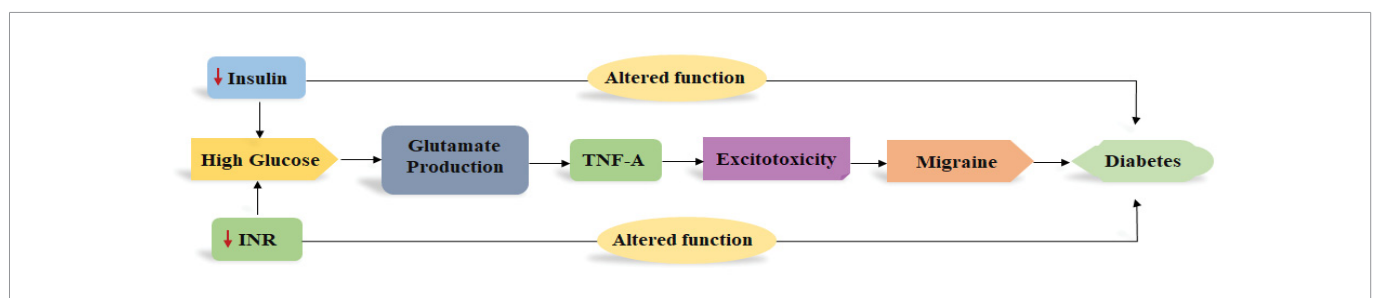


Figure 2: High Glucose possible risk factor as a link between migraine and diabetes: As seen in this flow chart, increased blood glucose levels are characterized by a decline (downward arrow) in insulin or reduced INR function. Higher glucose levels inside the brain drive glutamate production, which activates the TNF-A signaling cascade, culminating in glutamate excitotoxicity due to a positive feedback loop (hyperexcitability). Migraine is marked by neuronal hyperexcitability. Diabetes is characterized by altered insulin and INR (insulin receptor).

is a crucial component of migraineurs that is responsible for a variety of problems, one of which is increased glutamate synthesis. Glutamate binds to the mGluR2 to induce TNF- α production and TNF- α can potentiate excitotoxicity. We concluded that adhering to a strict low glycemic index diet can be an effective and dependable migraine-reduction approach.

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