

Heavy Metals Explain the Relation between Toxoplasma gondii, Influenza virus and COVID.19

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Heavy metals such as zinc responsible for many biological tasks in human body, and these functions disturb upon alteration of these essential metals, beside these positive roles, metals also induce many pathological problems. In this article we suggest the role of toxoplasma gondii as host for influenza virus that provide suitable environment to the virus to evade immune system. And according to hypothesis mentioned that; COVID.19 is mutant form of influenza virus, we said that slow spread of the pandemic among population with high prevalence of toxoplasmosis attributed to role of zinc in regulation of immunity, through protection of host cells from the virus and protection of parasites that hold viral colonies and prevent it spreads. Further studies recommended to check these hypothesizes.

Keywords: Zinc, Magnesium, Lead, Cadmium, Heavy Metals, Toxoplasma gondii, Influenza virus, COVID.19.

Introduction:

Toxoplasma gondii is one of the most common human zoonosis, infecting about a third of the world's population. Toxoplasmosis is generally benign and often goes unnoticed in immunocompetent individuals; however, non-specific flu-like symptoms, lymphadenopathy, and some rare complications might be associated with primary infection [1].

In December 2019, a series of acute atypical respiratory disease occurred in Wuhan, China. This rapidly spread from Wuhan to other areas. It was soon discovered that a novel coronavirus was responsible. The novel coronavirus was named as the severe acute respiratory syndrome coronavirus-2 (SARS-CoV-2, 2019-nCoV) due to its high homology (~80%) to SARS-CoV, which caused acute respiratory distress syndrome (ARDS) and high mortality during 2002–2003 [2].

Some people who have toxoplasmosis may feel as if they have the “flu” with swollen lymph glands or muscle aches and pains that may last for a month or more [3].

I suggest that *Toxoplasma gondii* parasitized by influenza virus, and this symbiotic relation decrease the pathogenesis of *Toxoplasma gondii* and increase the survival of influenza virus, then patients suffer from flu for longer than normal recovery period.

Metal ions are integral part of some viral proteins and play an important role in their survival and pathogenesis. Zinc, magnesium and copper are the commonest metal ion that binds with viral proteins. Metal ions participate in maturation of genomic RNA, activation and catalytic mechanisms, reverse transcription, initial integration process and protection of newly synthesized DNA, inhibition of proton translocation (M2 protein), minus- and plus-strand transfer, enhance nucleic acid annealing, activation of transcription, integration of viral DNA into specific sites and act as a chaperone of nucleic acid. Metal ions are also required for nucleocapsid protein-transactivation response (TAR)–RNA interactions .In influenza virus Cu, Ni, Pt, Zn bind to M2 protein , Zn, Mg, Mn, Co, bind to M1 peptide linker , and also Zn binds to Peptide CCHH motif , while in corona virus ZN also have three binding sites NS , p66 HEL and NS13 [4]. In toxoplasmosis Mg levels were found to be clearly decreased in the patients with chronic toxoplasmosis, whereas no change was observed in Zn levels [5].

Study done by Xiao S. et al showed that; Magnesium-dependent RNA binding to the PA endonuclease domain of the avian influenza polymerase [6], and we suggest that explain decrease of Mg level in chronic toxoplasmosis cases.

Zinc is crucial for normal development and function of cells mediating innate immunity, neutrophils, and NK cells. Macrophages also are affected by zinc deficiency. Phagocytosis, intracellular killing, and cytokine production all are affected by zinc deficiency. Zinc deficiency adversely affects the growth and function of T and B cells. The ability of zinc to function as an anti-oxidant and stabilize membranes suggests that it has a role in the prevention of free radical-induced injury during inflammatory processes [7].

Normal concentrations of Zinc in toxoplasmosis induce mild symptoms or even asymptomatic characters of this opportunistic disease.

Both magnesium and vitamin D are important to the immune system independently. Together, they may be beneficial in COVID-19 infection because magnesium is necessary to activate vitamin D [8]. Zinc help vitamin D to work inside the cells [9], Patients with coronavirus disease 2019 (COVID-19) had significantly low zinc levels in comparison to healthy controls, Zinc deficient patients developed more complications (70.4% vs 30.0%, $p = 0.009$) [10].

I hypothesized that Lead and Cadmium mutate Influenza virus and Produce: SARS COV-2 [11], and I disagree with study done by Martinez .O et al; whom suggest that *T. gondii* infection may be contributing to the high indices of behavioral changes, and suggest a possible interaction between chronic *T. gondii* infection and elevated blood lead levels on children's neurobehavior [12]. I suggest that only high lead levels are responsible for neurobehavior of children's.

The current data demonstrate that As, Cd, Hg, and Pb exposure is associated with respiratory dysfunction and respiratory diseases (COPD, bronchitis) [13], these metals may enhance viral replication.

The spread of toxoplasmosis is slower in societies where more people suffer from toxoplasmosis [14] , and this enhance our hypothesis about the origin of COVID.19 virus [11] , and hosting of *Toxoplasma gondii* to influenza virus.

Study done by Carvalho et.al; showed that; essential metal ($ZnCl_2$) protected the host cells and parasites against toxic effects of non-essential metals ($HgCl_2$ and $CdCl_2$) [15], and that may explain low spread of COVID.19 in communities with high number of *Toxoplasma gondii* cases.

Conclusion and recommendations:

As the virus attracted by the parasite, and eliminate it spreads, further more normal concentrations of zinc in toxoplasmosis help to diminish sequels of COVID.19. Experimental studies recommended to prove these postulations.

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