

Recurrent Urinary Tract Infection: Time to Recommend Weight Loss?

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We have read with great interest the article in this issue of the *Israel Medical Association Journal (IMAJ)* by Nseir and colleagues [1]. They observed an association between non-alcoholic fatty liver disease (NAFLD) and recurrent urinary tract infections (rUTIs). NAFLD is a chronic liver disease caused by hepatic fat accumulation in the absence of excessive alcohol consumption. NAFLD represents a spectrum of chronic liver diseases that range from simple steatosis to nonalcoholic steatohepatitis and cirrhosis [2]. Like the increasing prevalence of obesity and metabolic syndrome globally, NAFLD is considered among the most common chronic liver diseases worldwide and has become one of the leading indications for liver transplantation in adults [3].

Awareness of NAFLD as a multisystemic disease has increased and it is replacing viral hepatitis as the mainstay of clinical hepatology, especially with the advancement in treatment for hepatitis C virus using direct-acting anti-viral drugs. In addition, NAFLD is now widely encountered by various practitioners in different settings.

The pathogenesis and development of NAFLD is a complex and multifactorial process [4]. Insulin resistance from excessive accumulation of free fatty acids is thought to be a primary factor in the development of steatosis in most patients with NAFLD. Other factors may include

increased secretion of specific pro-inflammatory cytokines, mitochondrial dysfunction, oxidative stress, disorders in the metabolism of adipose tissue, microbiota alterations, and genetic factors [5].

A large body of literature currently exists to suggest that the clinical burden of NAFLD is part of a multisystem disease and not merely confined to the liver. In addition to the well-known association with metabolic syndrome, it has been clearly demonstrated that NAFLD is independently associated with an increased risk of cardiovascular disease, chronic kidney disease, type 2 diabetes, and possibly malignancies [6]. Moreover, in a recent literature search we found a wide spectrum of clinical conditions associated with NAFLD, and more studies are being conducted to confirm these findings. Of interest, the number of associations with infectious and inflammatory conditions are increasing.

The article by Nseir and co-authors in this issue of *IMAJ* [1] examined the association between NAFLD and recurrent urinary tract infections (rUTIs), one of the most commonly acquired bacterial infections in the inpatient and outpatient settings. In this well-designed retrospective study, NAFLD was showed to be significantly and independently associated with rUTIs in premenopausal women (odds ratio = 1.6, 95% confidence interval 1.3–2.0, $P = 0.04$). Although mechanisms underlying the association between these conditions has not been well examined, recent literature may shed light on several pathways that link between NAFLD and rUTIs. In addition to evidence from meta-analyses that revealed an increased prevalence of chronic kidney disease in patients with NAFLD [7], recent

evidence has shown that elevated body mass index appears to be associated with an increased risk for urinary tract infections and pyelonephritis [8]. Moreover, significantly increased risk of urolithiasis among patients with NAFLD was observed in a recent meta-analysis [9], a possible risk for increased recurrent urinary infection risk. Notably, emerging evidence suggests that altered immunity and low vitamin D concentrations are common among NAFLD patient [10–12]. Still, more investigations are needed to explain pathogenic pathways and mechanisms involved in acquiring rUTIs in NAFLD.

CONCLUSIONS

This is not the first time that NAFLD was reportedly associated with bacterial infections. NAFLD was associated with an increased risk of recurrent bacterial infections irrespective of metabolic syndrome in one study [13]. NAFLD was also associated with 30-day all-cause mortality in patients with community acquired pneumonia in a recent report [14].

These findings need to be confirmed and associations validated by prospective cohort studies, as this may have a paramount impact on disease morbidity as well as implications on clinical approach. Due to the associations of obesity and NAFLD with rUTI, one could assume a potential helpful effect and have another good reason to encourage lifestyle modification and weight loss in this regard.

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Capsule

Artificial memories

Activity patterns in distinct neural circuits eventually form coded memories during learning. In theory, replicating the same neural activity could recreate these memories without requiring the real-life learning experience. **Vetere** and co-authors showed how artificial memories can be created by stimulating brain regions. In optogenetics, light can be used to silence or activate proteins labeled with light-sensitive rhodopsins. With this technology, the authors identified the neural pathways that are involved in the formation of

“real” memories during an odor conditioning task. Mice will memorize a preference or aversion toward specific odors. In these experiments, animals that were conditioned through experience showed the same responses as animals that had an optogenetically implanted memory. The expression of both real and artificial memories depended on activity in a brain region called the basolateral amygdala.

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Eitan Israeli

Capsule

Galectin-3 in Alzheimer's disease

The role of the innate immune system and inflammation in Alzheimer's disease is currently undergoing scrutiny. Galectin-3 has been identified as a protein that is highly up-regulated in brain microglia during neurodegeneration and aging. **Boza-Serrano** and colleagues analyzed the potential role of galectin-3 in Alzheimer's disease pathology. They found that galectin-3 was highly up-regulated in brains from Alzheimer's disease patients, particularly in microglia associated with amyloid plaques. A similar distribution was seen in mouse models of Alzheimer's disease. Polymorphisms in the gene

encoding galectin-3 were associated with increased risk of Alzheimer's disease. In mouse models, reducing galectin-3 expression ameliorated plaque burden and improved cognitive behaviors. Furthermore, direct injections of galectin-3 and amyloid into wild-type mice induced amyloid aggregation in the hippocampus. Further work will be needed to confirm whether inhibiting galectin-3 could provide an approach to Alzheimer's disease treatment or prevention.

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Eitan Israeli

“Remember that fear always lurks behind perfectionism. Confronting your fears and allowing yourself the right to be human can, paradoxically, make you a far happier and more productive person”

David D. Burns (born 1942), American author and adjunct professor emeritus in the Department of Psychiatry and Behavioral Sciences at the Stanford University School of Medicine