Review Article

The Twin White Herrings: Salt and Sugar

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Abstract

India has the dubious distinction of being a hotspot for both diabetes and hypertension. Increased salt and sugar consumption is believed to fuel these two epidemics. This review is an in-depth analysis of current medical literature on salt and sugar being the two white troublemakers of modern society. The PubMed, Medline, and Embase search for articles published in January 2018, using the terms "salt" [MeSH Terms] OR "sodium chloride" [All Fields] OR "sugar" [All Fields]. India is world's highest consumer of sugar with one of the highest salt consumption per day. Increased salt intake is associated with increased risk of hypertension, left ventricular hypertrophy and fi brosis, cardiovascular events, renal stones, proteinuria, and renal failure. Increased sugar intake is directly linked to increased risk of obesity, fatty liver disease, and metabolic syndrome. Also, increased sugar intake may be indirectly related to the increased risk of type 2 diabetes. Both salt and sugar intake is directly linked to increased systemic and hypothalamic infl ammation, endothelial dysfunction, microangiopathy, cardiovascular remodelling, cancers, and death. High fructose corn is especially damaging. There is no safe limit of sugar consumption, as the human body can produce its own glucose. Being nature's gift to mankind, there is no harm in moderate consumption of salt and sugar, however, modest reduction in the consumption of both can substantially reduce the burden of non-communicable diseases. Public health interventions to facilitate this behavioural change must be instituted and encouraged.

Keywords: Cardiovascular disease, diabetes, hypertension, metabolic syndrome, non-communicable diseases, obesity, salt, sodium chloride, sugar

Introduction

India has the dubious distinction of being a hotspot for both diabetes and hypertension.[1] The current prevalence of diabetes and prediabetes in India is believed to be 10% and 15%, respectively.[2–4] Also Indians have the highest global rates of prediabetes progression to diabetes of 18% per year, as compared to only 2.5% in USA, 6% in Scandinavia, and 9% in China.[4,5] Diabetes onset is nearly two decades earlier in Indians, which is also driving the early onset of cardiovascular disease (CVD) epidemic in India. Cardiovascular events are the single most common cause of death in Indians, contributing more than 25% of all death among young Indian adults. Deaths due to cardiovascular events in Indians are more than the deaths caused by infectious diseases, cancers, and respiratory diseases.

The Government of India has reported that undiagnosed prevalence of non-communicable diseases (NCDs) is high for hypertension in India with the increase in disability-adjusted life year rate and included dietary risk factors in the Integrated Disease Surveillance Project.[6] Owing to nutrition transition, faulty eating habits (increased consumption of sugar and salt, diet high in energy, fat, refined grains, and other processed foods, sweets, and savoury snacks) and physical inactivity, there is a rapid rise in NCDs in India.[7,8]Also, global voluntary targets for selected NCD risk factors aim to reduce premature mortality from the main NCDs by 25% from 2010 to 2025 (referred to as the 25 × 25 target).[9]

Materials and Methods

References for this review were identified through searches of PubMed, Medline, and Embase for articles published till January 2018 using the terms "salt" [MeSH Terms] OR

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"sodium chloride" [All Fields] OR "sugar" [All Fields]. The reference lists of the articles thus identified were also searched. The search was not restricted to English-language literature.

Results

Nutritional composition and physiological significance of salt and sugar

Sodium ions are the major cation in the extracellular fluid (ECF) which contributes to the ECF osmotic pressure and its compartment volume. The renin–angiotensin system regulates the amount of fluid and sodium concentration in the body. Sodium contributes to the function of sodium–potassium pump, transmission of nerve impulses, and regulation of blood volume, blood pressure, osmotic equilibrium, and pH.

Chloride, as a component of the salt, is an essential electrolyte located in all body fluids responsible for maintaining acid/base balance, transmitting nerve impulses, and regulating fluid in or out of cells. Although the ill effects of chloride are unexplored in details, it is documented that both sodium and chloride are necessary for the development of hypertension.

Salt is double-fortified with iodine (prominent source being salt) as potassium iodide or potassium iodate and iron (also obtained from other dietary sources) as ferrous fumarate. The fortification is done on the basis of the mean recommended nutrient intake, losses from production to household, and bioavailability. Hence, over-consumption of salt may cause health issues associated with sodium, chloride, as well as toxicity of micronutrients being fortified in it.

Salt (sodium chloride) is used to flavour and preserve food, for curing meat, baking, thickening, retaining moisture, enhancing flavour, as a preservative, and used in food additives as well.[10]The physiological requirement for salt is <1 gm per day (sodium, Na = 400 mg) to maintain a balance of body fluids, transmission of nerve impulses, and normal cell function.[10,11]When salt intake is reduced in the body, there is a physiological stimulation of the renin–angiotensin system and the sympathetic nervous system.[12,13]Furthermore, research shows that reducing salt consumption to the World Health Organization's (WHO's) target (30% reduction by 2025) will not compromise iodine status.

Sugar is used for sweet taste and flavour. From a nutritional point of view, sugars are not essential nutrients because glucose can be synthesized by the body.[14]

Recommended daily allowance

The World Hypertension League and the International Society of Hypertension support WHO and the Food and Agriculture Organization (FAO) of the United Nations suggestion to reduce salt intake to 5–6 g/day as one of the top priority actions to tackle the global NCD crisis. National salt intake recommendations are between 5g and 8g of salt/day (sodium 2000–3200 mg).[13,15] Further, the levels of consumption >10 g per day are classified as very high and >15 g (sodium 6000 mg) per day as extreme.[15] The gold standard for sodium estimation is 24-hour urinary sodium excretion (24h UNa).[16]

There is no recommended daily allowance for sugar intake per day but is recommended to contribute not more than 10% of total energy intake.[17] The American Heart Association (AHA) has issued a scientific statement recommending that no more than 100 kcal/day for women and no more than 150 kcal/day for men from added sugars.[18,19]

Worldwide approaches and initiatives have been made to minimize the consumption of twin white herrings [Table 1].[12,16,20-23]

Present consumption of twin white herrings

Baseline survey for Shandong and Ministry of Health Action on Salt and Hypertension (SMASH) project among Chinese and Chennai Urban Rural Epidemiology Study (CURES) from India shows that salt consumption (9–12 g/day in most countries), in both hypertensive and normotensive participants is far exceeding the WHO recommendation.[12,19,21,24,25]

The mean percentage of energy from total free sugars is also higher than the WHO goal.[26] Data from the India sugar trade industry (2013) shows that India is the second largest (after Brazil) producer and largest consumer of sugar in the world.[16]

Dietary sources

As an indispensable food ingredient, salt is a commonly used medium for fortification of nutrients. Largely, it is added to food during or after food preparation. Sources of salt in the diet vary hugely among countries; in developed countries, 75% of salt comes from processed foods, whereas in developing countries, 70% comes from salt added during cooking, or at the table, and in sauces (e.g., soy sauce), spice mixes, seasonings, and pickles rather than pre-packaged prepared foods.[12,19]

Sugars are used as sweeteners, to make food palatable, to preserve foods, and to bestow certain characteristics to foods, such as viscosity, texture, body, colour, and flavours. As far the sources of sugar consumption in India is concerned, sugar-sweetened beverages (SSBs) contribute majorly along with soft drinks, high-fructose corn syrup (HFCS), junk food, and sweets among others.[14]

Understanding food labels, discussed in Table 2, is very crucial to estimate actual consumption.[14] The dietary consumption of salt and sugar can be reduced by wise selection of food items, altering cooking methods, choosing better alternatives, and natural flavouring food items in cooking. A few such nutritious tips are highlighted in Table 3, suggest alternatives to enhance taste/flavour of the food.[16,27-29]

Deleterious impacts of higher consumption: Hidden troublemakers

The deleterious impacts of higher consumption of these two hidden troublemakers are discussed in Table 4.[14,16,30-35] The damage caused by raised blood pressure (BP) is mainly through its effects on cardiovascular and kidney disease.[12,25] The INTERSALT study demonstrated a lower

Table 1: Worldwide approaches and initiatives minimizing the consumption of twin white herrings

Domain	Approach	Initiatives
Food production	New product development with no added salt or lowest content possible	Program of voluntary salt reduction in United Kingdom
	Universal and gradual reduction of the salt content of processed food	Spread awareness among consumers and the medical establishment regarding the ill effects of high sugar and salt intake
Environmental modulation/ regulatory measures	Making public health policy	2005: Establishment of World Action on Salt and Health (WASH)
	Formulate strict guidelines regarding recommended intake	2006: Food Standards Agency set target levels of salt for the food industry
	Encourage transnational food companies to manufacture healthy snacks and beverages	February 2010: Pan American Health Organization-WHO Regional Expert Group on cardiovascular disease prevention produced recommendations for a population-based approach to reduce dietary salt intake
	Decrease taxes on prices of fruits, vegetables, nuts, and other healthy foods	April 2010: Institute of Medicine released a report on strategies to reduce sodium intake in the United States
	Warning labels such as "Drinking beverages with added sugar(s) contributes to obesity, diabetes, and tooth decay" could be mandatory for SSBs	2011: UN General Assembly adopted a political declaration that committed member states to the prevention and control of NCDs
	Ensure that all imported food products are low in salt	India adopted a target 30% reduction in mean population salt consumption to prevent and reduce burden of non-communicable diseases by one-quarter by 2025 and reduced intake of free sugars to less than 10% of total energy intake as a global recommendation
Social health promotion/ consumer education	Awareness and understanding about the impact of salt on their health	Public health campaigns to encourage people to use less salt in their own food preparation
	Promoting a healthy lifestyle by health professionals through campaigns, programs, messages, warnings, and monitoring from health and media professionals as well as teachers	Restriction of advertisements for commercial foods on television
	Education about reading and understanding nutritional labels Behaviour-changing interventions	Inculcate healthy eating habits in children from early childhood
	National and international organizations are all taking initiatives to reduce salt intake by 30% by 2025 as part of the global action plan	Instead of sugar- and salt-loaded snacks, opt for fresh fruits and vegetables or home-made food
	Encourage low salt menu at social functions, religious gatherings	Read food labels and avoid intake of processed and packaged foods as much as possible
	Decreasing consumption of ultra-processed foods	Limit beverages containing added sugars: sucrose, glucose, fructose, maltose, dextrose, corn syrups, and honey

SSBs: Sugar-sweetened beverages, NCDs: Non-communicable diseases

Table 2: Understanding nutrient claims

What it says	What it means
Salt/sodium free	<5 mg sodium per serving
Very low sodium	≤35 mg sodium per serving
Low sodium	≤140 mg sodium per serving
Reduced sodium	At least 25% less than regular product
Lightly salted	At least 50% less than regular product
No added salt	No salt added during processing but may not be salt free
Sugar free	No direct sugar added but may contain artificial sweeteners

prevalence of hypertension in populations with a low urinary sodium excretion. An association between BP and a high-sodium intake has also been observed in children and adolescents.[32]

Similarly, limiting the sugar intake is expected to reduce BP and serum lipids.

Hypertension

Salt

One of the most important regulators of BP is exogenous salt intake. Excessive salt intake is a well-established risk factor for hypertension. A high-sodium diet draws water into the bloodstream increasing the volume of blood and subsequently BP which, in turn, magnifies both mesangial injury and glornerulosclerosis.[36] As it rises with age, limiting sodium intake becomes even more important each year.[10] The ill effects of excessive salt consumption have been summarized in Figure 1. Elevated BP is also a very important risk factor for cerebrovascular disease and CVD.[37] It is also known to cause cerebral edema, proteinuria, culminating in organ damage, and early death among stroke-prone spontaneously hypertensive rats (SHRSP).[38,39]

The Dietary Approaches to Stop Hypertension (DASH) have demonstrated a clear dose–response relationship in subjects with normal and mildly elevated BP.[12,40] A modest reduction in salt intake from approximately 10 g to 5 g per day over a duration of 4 or more weeks shows a significant effect on BP in both hypertensive and normotensive individuals, reduced deaths from stroke and coronary diseases, and prevents the incidence of antihypertensive therapy with small physiological increase in plasma renin activity, aldosterone, and noradrenaline and with no adverse effect on blood lipids, catecholamine levels, or renal function.[10,13,41] It is estimated that a reduction of 1 g/day would result in

Table 3: Sugar and salt alternatives

Ways/sources	Alternatives to salt	Alternatives to sugar
Spices/herbs	Asafoetida (heeng)	Ocimum tenuiflorum (tulsi)
	Black pepper (kali mirch)	Thymus vulgaris (ajavaayan ki patti)
	Red capsicum pepper (laal Shimla mirch)	Saffron (kesar)
	Green capsicum pepper (hari Shimla mirch)	Cardamom (elaichi)
	Oregano	Ginger
	Basil	Mango ginger (Uttrakhand)
	Soy	Vanilla
	Sage	Cinnamon
	Bay leaves	Clove
	Curry patta	
Seasonings	Vinegar	Sugar-free products like stevia (in acceptable daily intake)
	Onion	
	Garlic	
	Ginger	
	Lemon	
Variants of food stuffs	Home-made chutneys/sauces	Skimmed buttermilk
		Tender coconut water
		Low-fat milk
		Lemon water
		Natural-flavoured fruits and vegetables
Cooking methods	Steaming	Steaming
	Boiling	Boiling
	Baking	Baking
	Roasting	Roasting
	Grilling	Grilling

Table 4: Possible deleterious impacts of higher consumption of salt and sugar

Salt	Sugar
Hypertension	Obesity and visceral fat adiposity
Left ventricular hypertrophy and fibrosis	Insulin resistance
Stroke	Type 2 DM
Abdominal aortic aneurysm (AAA)	Metabolic syndrome
Proteinuric renal disease	Hypertriglyceridaemia
Disordered mineral metabolism	Hyperuricaemia
Oxidative stress	Fatty liver disease
Endothelial dysfunction	Cardiovascular disease
Renal stones	Tooth decay
Osteoporosis	
Increased severity of asthma	
Carcinoma stomach	

reduction in BP of 0.8/0.5 mmHg, 5% stroke risk, and 3% ischaemic heart disease risk.[42] High-quality evidence in non-acutely ill adults shows reduction in BP with no adverse effect on blood lipids, catecholamine levels, or renal function.

Sugar

Hyperinsulinaemia, caused by sugar intake, raises BP, in part, by decreasing sodium and water excretion in the kidneys, and directly vasoconstricting blood vessels. High sugar intake, particularly fructose, promotes atherogenesis through the interaction of receptors on the blood vessel wall, alter lipid metabolism unfavourably, which promotes inflammation and oxidative stress. Fructose, in particular, is associated with cardiorenal disease epidemic.[43]

Cardiovascular disease

Salt

Increased 24h UNa is associated with an increased risk of cardiovascular morbidity and mortality, impaired cardiac diastolic function, especially in patients with diabetes.[44] According to the WHO, 62% of all strokes and 49% of all coronary heart disease (CHD) events are attributable to high BP. Overconsumption of salt causes systolic contractile dysfunction due in part to hypertension, the hydrostatic effect of salt increases the size of the muscle mass, increases cardiac muscle hypertrophy, and is responsible for excess deposition of collagen and fibrous tissue causing thickening of the coronary arteries and impairing coronary perfusion. It can impair myocardial function by the increase in cardiac output that results in part from the salt-induced rise in right auricular pressure.[45] It may induce severe inflammatory reactions through augmentation of T-helper 17 cells and their highly inflammatory cytokines.[46] Over consumption of salt carries a higher risk of cerebrovascular disease especially in overweight individuals.[47] The positive correlation between salt intake and high-sensitivity C-reactive protein may be evidenced to contribute inflammatory damage in congestive heart failure.[48] A high salt intake is associated with myocardial hypertrophy, independent of blood pressure.

The long-term Trials of Hypertension Prevention (TOHP) has shown that reduction in salt intake leads to reduction in the

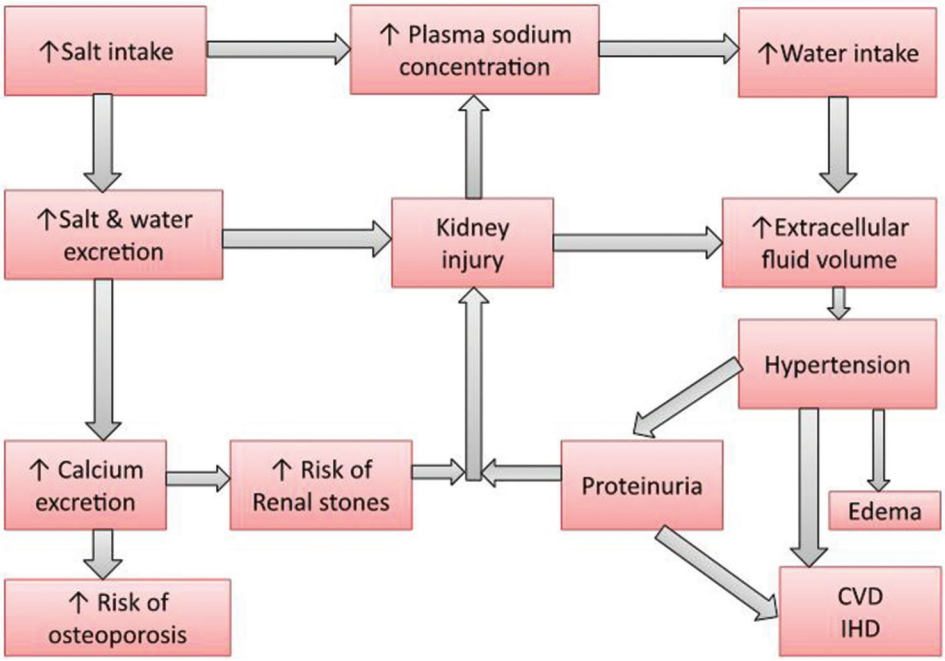

Figure 1: Ill effects of excessive salt consumption

burden as well as mortality from CVD even after adjusting for several confounding factors. Salt reduction leads to reduced incidence of stroke as well as reduced incidence and mortality from CHD. It also prevents fluid retention and symptomatic deterioration in people with heart failure.[49–51]

Sugar

Sugar contributes to obesity through their caloric load. Sugar, 50% of which is fructose may increase inflammation and oxidative stress. Similarly, a higher intake of added sugar (soft drinks, fruit drinks, desserts, sugars and jellies, candy, and ready-to-eat cereals) and regular consumption of SSB is associated with obesity and associated diseases.[17,52–54] It causes elevation of BP and the lowering of high-density lipoprotein (HDL)-cholesterol levels, abdominal fat deposition, and cause insulin resistance, develop interstitial fat deposition, and fibrosis in liver.[33,54,55] Excess sugar intake in hypercaloric diet have postprandial triglyceride-raising effect, may increase ectopic fat depots particularly in the liver and in muscle fat which may further cause fatty liver disease and increase cardiometabolic risk.[18,56,57] Fructose is metabolized primarily in the liver and enhances lipogenesis and the production of uric acid.[17,18,58] Short-term mechanistic studies have shown that excess fructose ingestion can result in additional cardiometabolic effects due to increased hepatic de novo lipogenesis (DNL), accumulation of visceral adiposity and ectopic fat, and production of uric acid.[59]

LV hypertrophy

Salt

Salt intake is independent predictor of the extent of left ventricular (LV) hypertrophy, a well-known risk factor for premature CVD and sudden cardiac death. High sodium and low potassium inhibit the sodium pump, increase intracellular sodium, and drive calcium into cells which ultimately induce vascular smooth muscle contraction and increased peripheral vascular resistance. It may sensitize the heart to the hypertrophic stimulus of pressure load[60] and accelerate the post infarction ventricular remodelling.[61] A moderate reduction in salt intake is known to cause regression of LV hypertrophy.[62]

Sugar

In a study on hypertensive rat models, a high fructose intake increased LV wall thickness, decreased LV contractile function, and increased mortality. Limited evidence shows that high-sugar diets may affect myocardial antioxidant enzymes and hydrogen peroxide levels causing diet-induced oxidative stress and heart failure.[63,64]

Diabetes and insulin resistance

Salt

As determined by 24h UNa, in individuals with diabetes, high dietary salt intake may be a risk factor for microalbuminuria, particularly in overweight individuals. Sodium and volume retention in diabetes mellitus could activate factors responsible for the progression of diabetic microangiopathy. For patients with diabetes and associated hypertension, renal disease, or CVD, dietary sodium intake should be restricted to <2,000 mg/day.[65,66]

Maintaining BP at or below target levels leads to fall in BP in individuals in patients with diabetes due to sodium retention and enhanced vascular reactivity to angiotensin II.[67,68]

Sugar

A study demonstrated 1.1% increase in the prevalence of diabetes as a result of the extra uptake of 150 kcal from sugars

per person per day, which is the equivalent of approximately 35 g of sugar.[69] Because of the high glycaemic load, it may increase the risk of diabetes by causing insulin resistance and also through direct effects on pancreatic islet cells. The excess energy intake leading to overweight and obesity with parallel and dramatic increase in worldwide diabetes and insulin resistance prompts the need to explore nutritional links to diabetes.[18] Sugar intake may exacerbate the later stage of type 1 diabetes development; SSBs may be especially detrimental to children with genetic predisposition to type 1 diabetes.[70] The excessive fructose, HFCS, and SSBs consumption plays a role in the epidemics of insulin resistance, visceral adiposity, type 2 diabetes mellitus (T2DM), and associated morbidities.[19,71–74] It may adverse lipid parameters, inflammation, and clinical CHD, exacerbate levels of inflammatory biomarkers such as C-reactive protein linked to T2DM and CVD risk, induce glucose intolerance and insulin resistance. Inflammation is known to influence atherosclerosis, plaque stability, thrombosis, hyperuricaemia, incidence of developing gout, T2DM, and cardiovascular risk independently of obesity. SSBs may contribute to T2DM and cardiovascular risk in part by their ability to induce weight gain, but an independent effect may also stem from the high amounts of rapidly absorbable carbohydrates such as any form of sugar or HFCS, the primary sweeteners used in SSBs.[75–77]

Once the immune system has been activated and the body has begun the autoimmune attack on the beta cells, the total amount of sugar that a child consumes may increase type 1 diabetes risk. Sugar may be toxic to the beta cell, and intermittent exposure to high levels of dietary sugars may directly induce beta cell apoptosis and reduce normal beta cell proliferation.[70]Several high-sugar-induced changes in mRNA levels are indicative of peripheral insulin resistance. The susceptibility gene hexokinase C may be downregulated by high-sugar feeding, suggesting that glucose disposal through glycolysis might be impaired. An expression of the genes encoding the gluconeogenic enzymes PEPCK and fructose-1,6-bisphosphatase may be upregulated by high-sugar feeding. The hepatic metabolism of fructose may contribute to glycation and diabetic complications inducing insulin resistance and chronic hyperlipidaemia.[78,79]

Metabolic dysfunction

Sugar

Fructose metabolism in the liver may lead to ATP depletion and increase in uric acid through ATP degradation to AMP, which in turn, may lead to endothelial dysfunction, hypertension, insulin resistance, hypertriacylglycerolaemia, obesity, and inflammation.[18,77,80–83] It can cause hypertension, promote accumulation of visceral adipose tissue (VAT) and ectopic fat due to elevated hepatic DNL resulting in the development of high triglycerides and low HDL cholesterol.[80] It being positively associated with TG concentrations.[81] Abdominal adiposity, particularly VAT, is linked to the pathogenesis of diabetes and CVDs.[84] Limited evidence suggests that excess added sugar intake under hypercaloric diet conditions likely increases ectopic fat depots, particularly in the liver and in muscle fat.[53] It may cause fatty liver and high levels of free fatty acids. High doses of fructose (>50 g/day at least) in humans have been implicated in elevated BP mediated by high levels of non-esterified fatty acid (NEFA). Increased portal delivery of NEFAs increase hepatic glucose production, impair beta cell function, and cause hepatic steatosis.[16,85] It may increase DNL, promote dyslipidaemia, decreases insulin sensitivity, and increases visceral adiposity in overweight/obese adults.[86] It may lead to the development of hepatocellular carcinoma.[87]

Low-fructose diets coupled with mild purine restriction may improve weight and reduce CVD risk.[79]

Obesity

Salt

Salt loading increases circulating ghrelin production (a gut hormone that increase appetite) and this may be the underlying mechanism of salt-induced obesity especially childhood obesity[32] and modest weight gain in adults.[18,19,80] The obesity prone rats on high salt displayed adipocyte hypertrophy and increased leptin production.[88,89]

Sugar

The chronic stress combined with a high fat-sucrose diet, leads to abdominal obesity by releasing a sympathetic neurotransmitter, neuropeptide Y (NPY), directly into the adipose tissue. It stimulates endothelial cell (angiogenesis) and preadipocyte proliferation, differentiation, and lipid-filling (adipogenesis). It results in metabolic syndrome-like symptoms with abdominal obesity, inflammation, hyperlipidaemia, hyperinsulinaemia, glucose intolerance, hepatic steatosis, and hypertension.[90]

Kidney disease and stones

Salt

High dietary salt intake presents a major challenge to the kidneys which have to work to excrete this load. It may have detrimental effects on glomerular haemodynamics, inducing hyperfiltration and increasing the filtration fraction and glomerular pressure. Salt intake plays a role in endothelial dysfunction, albuminuria, and kidney disease progression. It is proposed that high sodium intake can blunt the antiproteinuric effect of ACE inhibition and calcium antagonists in proteinuric hypertensive patients. A low salt intake has been shown to reduce BP and proteinuria in subjects with non-diabetic nephropathy.[86,91]

The PREVEND (Prevention of REnal and Vascular ENd stage Disease) study documented a continuous positive relation between 24h UNa and albuminuria.[89]The proximal tubular reabsorption show sensitivity to dietary salt in diabetic rats. This renders the tubuloglomerular feedback signal sensitive to dietary salt and leads to a paradoxical effect of dietary salt on glomerular filtration rate (GFR) in diabetes mellitus. Glomerular hyperfiltration places a pathologic stress on the diabetic kidney; hence the advice to diabetic patients to curtail their salt intake.[89,92,93]In patients with type 1 diabetes, sodium is independently associated with all-cause mortality and end

Table 5: Possible deleterious effects of salt and sugar in other disease conditions

Salt	
Edema	Retention of sodium chloride lead to edema in proteinuric edematous patients
	Increased loss of test animals as a result of the maximum decrease in the local cerebral blood flow and sharply pronounced brain swelling
	Restricted consumption reduced the extent of cerebral ischaemia, brain swelling effect, increased the renal perfusion, and diuresis levels
Cancer	High intake of salt is evidenced to be a risk factor for stomach cancer, nose, throat, nasopharyngeal cancer, and kidney cancer
	It is a significant risk factor for gastric cancer, found to be strong in the presence of *Helicobacter pylori* infection with atrophic gastritis
	May stimulate proliferation of bowel epithelium enhancing colorectal carcinogenesis
	DNA damage, DNA mutation, and carcinogenesis suggest that DNA damage can be a biological link between diabetes and cancer
Osteoporosis	Increasing salt intake produces changes in the chemical composition of urine which may predispose to kidney stone formation and increase hydroxyproline excretion indicating increased bone resorption
	Sodium restriction reduces calcium excretion which may reduce bone demineralization and hip fractures
Asthma	Smooth-muscle reactivity and bronchial hyperresponsiveness to methacholine is increased in the arteries as well as bronchi by higher salt intake
	The dietary salt loading enhances airway inflammation following exercise in asthmatic subjects and such small salt-dependent changes in vascular volume and microvascular pressure might have substantial effects on airway function following exercise leading to fall in circulating catecholamine concentrations
	Changes in plasma adrenaline concentration modify bronchial reactivity 5 and could account for up to half the change in bronchial reactivity that occurs with salt loading
	An increase in circulating sodium-potassium ATPase inhibitors due to an increase in salt intake may increase inflammatory cell and hence airway responsiveness
	Adoption of a low-sodium diet may improve lung function, asthama symptoms, lower methacholine reactivity, a reduction in bronchodilator consumption, increased peak flow and forced expiratory volume in humans and decrease bronchial reactivity, and decreases bronchoconstriction in response to exercise in adults with asthma
Sugar	
Non-alcoholic fatty liver disease	Hepatic metabolism of fructose favors de novo lipogenesis and ATP depletion
	Increased hepatic mRNA expression of fructokinase and fatty acid synthase
	Correlated with intrahepatic fat accumulation
	Lower steatosis grade, higher fibrosis stage, increased hepatic inflammation, and hepatocyte ballooning
	Additional feature of the metabolic syndrome: hepatic insulin resistance regular SSB consumption is associated with greater risk of fatty liver disease, particularly in overweight and obese individuals
Immune function	High-sugar diet may induce changes in gut microbiota composition, alter host homeostasis, and promote AIEC gut colonization in genetically susceptible mice supporting the multifactorial aetiology of Crohn's disease (CD)
Tooth decay	Associated with development of dental caries
	Stimulate bacteria to produce acid and lower the pH<5% energy from sugar lower dental caries and protect dental health throughout life (WHO)
Uric acid	Sugar causes mitochondrial oxidative stress that stimulates fat accumulation independent of excessive caloric intake
	Fructose elevates uric acid which drives up blood pressure by inhibiting the nitric oxide (NO) in blood vessels. NO suppression leads to increases in blood pressure
	May cause endothelial dysfunction
Ageing	Specifically dietary fructose increases DNL, promotes dyslipidaemia, decreases insulin sensitivity, and increases visceral adiposity in overweight/obese adults
	Sugar is noteworthy as a substance, releases opioids and dopamine and thus might be expected to have addictive potential
Behaviour/ cognition	Sugar intake is inversely associated with cognitive performance, lower word list learning score, poorer performance in visual spatial memory, working memory, scanning and tracking, executive function, the global composite and the Mini-Mental State Examination in diabetic individuals
	Leads to higher levels of C-reactive protein (marker of low-grade inflammation), reduced hippocampal-dependent memory, and sensitivity to interoceptive signals
	Association between HFS consumption and poorer hippocampal function in human participants may be related to impaired regulation of energy intake via less accurate tracking of prior food intake and reduced sensitivity to hunger and satiety signals
	It can influence brain structure and function via regulation of neurotrophins, reduce hippocampal level of BDNF, and spatial learning performance
	A metabolic-brain-negative feedback pathway and stress-dampening effects of sugar may explain differences in disease subtypes, such as major depression
	Insulin resistance status induced by high fructose intake and insulin resistance syndrome is linked to cognitive decline and neurodegeneration
	May exacerbate AD-like cognitive impairment and cerebral amyloid
	Association between high fructose consumption and increased risk of cognitive impairment could be mediated by high levels of UA caused by high fructose intake
	Reduce sugar intake may prevent cognitive impairment

stage renal disease. A syndrome of edema and renal failure with significant histologic changes in the kidneys and certain other organs are observed in rats consuming high levels of NaCl.[94,95] Changes in salt intake may influence urinary excretion of proteins in patients with essential hypertension, or diabetic and non-diabetic nephropathies.[96] The high salt intake worsens metabolic acidosis in patients with renal insufficiency.

Higher the salt intake, greater the urinary calcium excretion and there is significant direct relation between urinary sodium excretion and reduction in hip bone density.[89]Nurses' Health Study found that lower sodium intake was associated with a lower risk for decline in estimated GFR compared with women in the highest quartile of sodium intake.[59]The salt restriction improves glomerular hyperfiltration, kidney enlargement, and microalbuminuria in an experimental rat model of diabetes.[97]Restricting salt and water intake can effectively treat fluid overload in diabetic peritoneal dialysis patients, which may help reduce the use of hypertonic glucose solution. Avoid excessive salt consumption as a preventive measure for avoiding each type of renal calculus formation specially calcium oxalate stones.[98,99]

Health effects of twin white herrings in other disease conditions

The deleterious effects of salt and sugar have also been evidenced in other disease conditions [Table 5].[100-117]

Conclusion

Salt and sugars, though an integral part of daily diets, can be termed as seemingly innocuous twin white herrings, owing to their strong association with the risk of various NCDs. Being nature's gift to mankind, there is no harm in their moderate consumption. The measures to limit their intake provide comprehensive, accessible, community-based, preventive, curative, and rehabilitative measures for NCDs.

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Conflicts of interest

There are no conflicts of interest.

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