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A Call for a Modern Satyagraha Against Metabolic Syndrome

ABSTRACT

Objective: In 1923, while India was engaged in the Flag Satyagraha movement for independence, the medical community witnessed the discovery of insulin and the early recognition of metabolic syndrome (MetS) by Swedish physician Eskil Kylin. This article draws parallels between the historical Satyagraha movement and the current fight against MetS, advocating for a comprehensive and integrated approach to managing this syndrome. We explore the multifaceted role of sodium-glucose cotransporter-2 inhibitors (SGLT2i) in managing MetS, emphasizing their cardioprotective and renoprotective benefits.

Materials and methods: A detailed review of existing literature on MetS, its definitions, prevalence, and management strategies was conducted. The therapeutic potential of SGLT2i was examined through a meta-analysis of randomized controlled trials (RCTs) to assess their impact on key components of MetS, including fasting plasma glucose, waist circumference (WC), blood pressure, body weight, and uric acid levels.

Results and conclusions: SGLT2is, including empagliflozin, dapagliflozin, and canagliflozin, demonstrated significant efficacy in improving several components of MetS. Notably, these agents reduced fasting plasma glucose by up to 30.02 mg/dL and WC by 1.28 cm, while also providing modest reductions in systolic blood pressure and body weight. Additionally, SGLT2is were associated with significant reductions in uric acid levels, contributing to their renoprotective effects. Despite the minimal impact on high-density lipoprotein (HDL) cholesterol levels, SGLT2is showed broad cardiometabolic benefits, including anti-inflammatory effects and modulation of sympathetic nervous system activity. Public health initiatives must also prioritize lifestyle modifications and early detection to curb the rising prevalence of this condition. (Clin Diabetol 2025; 14, 1: 50–55)

Keywords: metabolic syndrome, SGLT2 inhibitors, cardioprotection, renoprotection, public health, diabetes, cardiovascular disease, hypertension, insulin resistance

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Introduction

In 1923, India saw a powerful movement of nonviolent resistance known as the Flag Satyagraha, led by Ballav Bhai Patel in Nagpur — a significant moment in

Table 1. Definitions of Metabolic Syndrome

Organization	Year	Mandatory criterion	Additional criteria	Diagnosis
WHO [4]	1998	Insulin resistance	Waist-hip ratio [> 0.90 (M), > 0.85 (F)], BMI > 30 kg/m^2, TG ≥ 150 mg/dL, HDL < 35 mg/dL (M), < 39 mg/dL (F), BP ≥ 140/90 mmHg, microalbuminuria	Insulin resistance + ≥ 2 other criteria
EGIR [5]	1999	Hyperinsulinemia (plasma insulin > 75th percentile)	WC ≥ 94 cm (M), ≥ 80 cm (F), TG ≥ 177 mg/dL, HDL < 39 mg/dL, BP ≥ 140/90 mmHg	Hyperinsulinemia + ≥ 2 other criteria
AACE [6]	2003	None	BP ≥140/90 mmHg, fasting glucose 110–125 mg/dL, TG ≥ 150 mg/dL, family history of diabetes, hypertension, or CVD, sedentary lifestyle	≥ 2 criteria plus family history or sedentary lifestyle
IDF [7]	2005	Central obesity [WC ≥ 94 cm (M), ≥80 cm (F)]	Fasting glucose ≥100 mg/dL, TG ≥ 150 mg/dL, HDL < 40 mg/dL (M), <50 mg/dL (F), BP ≥ 130/85 mmHg	Central obesity + ≥ 2 other criteria
NCEP ATP III [8]	2000, revised 2005	None	WC > 40 inches (M), > 35 inches (F), fasting glucose ≥ 100 mg/dL, HDL < 40 mg/dL (M), < 50 mg/dL (F), BP ≥ 130/85 mmHg	≥ 3 criteria

AACE — American Association of Clinical Endocrinologists; BMI — body mass index; BP — blood pressure; CVD — cardiovascular disease; EGIR — European Group for the Study of Insulin Resistance; F — female; HDL — high-density lipoprotein; IDF — International Diabetes Federation; M — male; NCEP ATP III — National Cholesterol Education Program Adult Treatment Panel III; TG — triglycerides; WC — waist circumference; WHO — World Health Organization

the nation's struggle for independence [1]. In the same year, medical science celebrated a milestone with the awarding of the Nobel Prize for the discovery of insulin, forever transforming the management of diabetes [2]. However, a lesser-known yet profoundly important development from 1923 also merits attention: the identification of metabolic syndrome (MetS) by Swedish physician Eskil Kylin, who described a pathological triad of hypertension, hyperglycemia, and hyperuricemia [3]. This syndrome, first observed over a century ago, continues to pose a significant threat to global health, and its growing prevalence demands a robust response.

As we reflect on the enduring spirit of resistance embodied by the Satyagraha movement, it is time to channel that same energy into combating MetS, which has emerged as a silent epidemic. Just as the Satyagraha sought to dismantle colonial oppression, our modern "Satyagraha" must be directed against the interlinked pathologies that constitute MetS, which collectively increase the risk of cardiovascular diseases (CVD), diabetes, and other life-threatening conditions.

The challenge of metabolic syndrome

MetS is a constellation of interrelated risk factors that includes central obesity, insulin resistance, dyslipidemia, hypertension, and hyperuricemia. These factors collectively elevate the risk of developing CVD and type 2 diabetes (T2D), making MetS a significant public health concern. The World Health Organization (WHO) first conceptualized MetS in 1998, emphasizing insulin resistance as a mandatory criterion alongside obesity, dyslipidemia, and hypertension [4]. Subsequent definitions by the European Group for the Study of Insulin Resistance (EGIR) in 1999 [5], the American Association of Clinical Endocrinologists (AACE) in 2003 [6], the International Diabetes Federation (IDF) in 2005 [7], and the National Cholesterol Education Program Adult Treatment Panel III (NCEP ATP III) in 2000 [8], have further refined the diagnostic criteria, each adding nuances based on regional and clinical perspectives. Despite the variations in definitions, the prevalence of MetS is consistently high, particularly in urban populations and among women. Studies in India suggest that the age-adjusted prevalence of MetS is approximately 25%, with higher rates in women compared to men [9]. This high prevalence, coupled with the syndrome's role as a precursor to several chronic conditions, underscores the need for heightened awareness and more effective screening and management strategies. The clustering of risk factors, particularly in populations like the Indian Armed Forces, where fitness levels are typically high, highlights the insidious nature of MetS and the importance of early intervention [10]. In addition, recent research highlights that anthropometric measures, such as waist, hip, and mid-thigh circumferences, can serve as easy and inexpensive markers for predicting T2D, even in resource-constrained settings, thereby reinforcing the importance of early detection and intervention in populations at risk [11].

Table 1 summarizes the various definitions of MetS, highlighting the differences in mandatory and additional criteria across the major health organizations.

Recent studies underscore the importance of a comprehensive approach to the management of MetS, which should address not only hyperglycemia but also other components like hyperuricemia and hypertension. Among the therapeutic strategies that have shown promise is the use of sodium-glucose cotransporter-2 inhibitors (SGLT2i). These agents, initially developed for the management of T2D, have demonstrated pleiotropic benefits that extend beyond glycemic control.

SGLT2 inhibitors: a comprehensive approach to metabolic syndrome

SGLT2i have increasingly been recognized for their multifaceted role in managing MetS, a condition characterized by a cluster of interrelated risk factors, including insulin resistance, central obesity, dyslipidemia, hypertension, and hyperuricemia. In a comprehensive meta-analysis [12] involving 26,427 patients, SGLT2i demonstrated significant efficacy in improving several key components of MetS. Specifically, SGLT2i, including dapagliflozin and empagliflozin, were associated with a mean reduction in fasting plasma glucose (FPG) of up to 30.02 mg/dL at higher doses (10 mg), while lower doses (2.5 mg) showed a minimal impact on FPG. Furthermore, these agents reduced WC by an average of 1.28 cm, highlighting their beneficial effects on central obesity, a core feature of MetS [12].

In addition to glycemic control, SGLT2i have shown a modest yet meaningful impact on systolic blood pressure (SBP), with reductions averaging 1.37 mmHg. Notably, dapagliflozin exhibited a more pronounced effect on SBP compared to empagliflozin, possibly due to differences in the number of randomized controlled trials (RCTs) analyzed and the baseline characteristics of the study populations. Although the reduction in diastolic blood pressure (DBP) was not statistically significant, the overall cardiometabolic profile of patients treated with SGLT2i improved significantly [12].

SGLT2i also exert beneficial effects on body weight (BW) and uric acid (UA) levels, both of which are crucial in the management of MetS. The use of SGLT2i resulted in an average weight loss of 1.79 kg, which is particularly important given the role of obesity in the pathogenesis of MetS. Additionally, these inhibitors significantly reduced UA levels by 1.03 mg/dL, with dapagliflozin showing a more substantial effect compared to empagliflozin [12]. This reduction in UA is clinically relevant, given the strong association between hyperuricemia and both MetS and CVD.

Despite these promising outcomes, the effect of SGLT2i on high-density lipoprotein (HDL) cholesterol was not significant, as indicated by a non-significant change in HDL levels across the analyzed studies [12]. This finding contrasts with the improvements observed in other MetS components and may reflect the heterogeneity in the study designs, patient populations, and treatment durations included in the analysis.

The mechanisms by which SGLT2i improve MetS components are multifactorial and include enhanced glucosuria, osmotic diuresis, natriuresis, and modulation of key metabolic pathways. These effects contribute to improvements in insulin sensitivity, blood pressure regulation, and lipid metabolism, making SGLT2i a valuable tool in the integrated management of MetS [13]. Furthermore, the upregulation of glucose transporter 9, which facilitates UA excretion in the kidneys, and the modulation of genes involved in lipid metabolism, such as peroxisome proliferator-activated receptor alpha (PPAR-) and adenosine monophosphate-activated protein kinase (AMPK), further underscore the broad cardiometabolic benefits of these agents [14, 15].

SGLT2i offer a comprehensive approach to managing MetS by targeting multiple risk factors simultaneously. While the improvements in individual MetS components may be modest, the cumulative benefits, particularly in reducing cardiovascular risk and improving overall metabolic health, position SGLT2i as a cornerstone in the treatment of MetS. Further research, particularly in the form of long-term RCTs, is warranted to fully elucidate the potential of SGLT2i in comparison to existing therapeutic strategies and lifestyle interventions.

A call for action: a modern Satyagraha

The parallels between the historical Satyagraha movement and the modern fight against MetS are compelling. Just as the Satyagraha movement was grounded in the principles of truth and nonviolent resistance, the contemporary battle against MetS must be rooted in scientific evidence and a commitment to holistic, patient-centered care. This new "Satyagraha" calls for healthcare providers to adopt an integrated approach that addresses the multifactorial nature of MetS.

Furthermore, this movement should extend beyond the clinic and into the community. Public health initiatives that promote lifestyle modifications — such as healthy diets, regular physical activity, and weight management — are essential in preventing the onset of MetS. Additionally, increasing public awareness about the condition and its long-term risks is crucial for early intervention and effective management.

MetS, once a debated concept, is now universally acknowledged as a critical public health issue both globally and in India. MetS is characterized by a cluster of risk factors, including central obesity, insulin resist-

Table 2. Recommendations for Physical Activity to Prevent and Manage Metabolic Syndrome [16–18]

Exercise type	Minimum recommendation	Optimal recommendation
Endurance exercises	150 min/week of moderate-intensity aerobic activity (e.g., 30 min/day, 5 days/week) or 75 min/week of vigorous-intensity activity	300 min/week of moderate-intensity aerobic activity (e.g., 60 min/day, 5 days/week) or 150 min/week of vigorous-intensity activity
Muscle-strengthening	Exercises involving major muscle groups on 2–3 days per week	Exercises involving major muscle groups on 2–3 days per week
Flexibility exercises	Gentle stretching (including yoga) for 5–10 min before and after exercise sessions	Gentle stretching (including yoga) for 5–10 min before and after exercise sessions
Lifestyle modifications	Incorporate physical activity into daily routines, such as using stairs, walking, cycling, and standing during phone calls	Maintain an active lifestyle with a conscious effort to reduce sedentary habits and integrate more physical movement into daily activities

Table 3. Dietary Guidelines for the Prevention and Control of Metabolic Syndrome [17, 19–21]

Nutritional element	Guideline
Total fats	Less than 30% of daily calories, preferably under 20%
Saturated fats	Less than 10% of daily calories, preferably under 7%
Trans-fatty acids	Should be eliminated from the diet
Polyunsaturated/monounsaturated fats	Polyunsaturated fats up to 10% of calories, monounsaturated fats 10–15%
Refined sugars	Less than 10% of daily caloric intake
Salt	Less than 5 grams per day
Dietary cholesterol	Less than 300 mg per day
Dietary recommendations	Emphasize whole grains, legumes, fruits, vegetables, and low-fat dairy products. Minimize gravied, fried, creamed, and sugared foods

ance, dyslipidemia, hypertension, and hyperuricemia, all of which significantly elevate the risk of CVD and T2D. Given the widespread prevalence and serious health implications of MetS, it should be a primary focus for public health policymakers and healthcare professionals.

Preventing and managing MetS effectively requires two core strategies: encouraging regular physical activity and maintaining a healthy diet. Public health guidelines emphasize the necessity of these lifestyle modifications. Physical activity recommendations, outlined in Table 2, suggest a minimum of 150 minutes per week of moderate-intensity aerobic exercise, such as brisk walking, or 75 minutes of vigorous-intensity activity. For those seeking optimal health benefits, increasing this to 300 minutes per week of moderate exercise or 150 minutes of vigorous exercise is advisable. Additionally, muscle-strengthening exercises should be incorporated into routines 2 to 3 times a week, focusing on major muscle groups. Flexibility exercises, including yoga, should also be practiced regularly to improve overall physical health [16–18].

Equally important is dietary management, as detailed in Table 3. The guidelines recommend a balanced diet where total fat intake is limited to less than 30% of daily calories, with an emphasis on polyunsaturated and monounsaturated fats. Saturated fats should constitute less than 10% (preferably under 7%) of total calories, and trans-fatty acids should be eliminated entirely. Refined sugars should make up less than 10% of caloric intake, and daily salt consumption should be restricted to under 5 grams. A diet rich in whole grains, legumes, fruits, vegetables, and low-fat dairy products is strongly advised, while foods high in cholesterol and unhealthy fats should be minimized [17, 19–21].

Public health initiatives should extend beyond individual counseling and include community-wide efforts to promote an active lifestyle and healthy eating habits. Encouraging simple lifestyle changes, such as using stairs instead of elevators, opting for walking or cycling instead of driving, and standing while on the phone, can significantly aid in the prevention of MetS.

Early detection of MetS is also crucial. Regular screening for central obesity, particularly through WC measurements by healthcare workers, provides an effective and straightforward method for identifying individuals at risk.

Table 4. Beneficial Effects of SGLT2 Inhibitors on Cardiometabolic Health [15, 22]

Cardiometabolic aspect	Impact of SGLT2 inhibitors
Blood pressure	Reduction in systolic BP (approx. -1.37 mmHg)
	Greater reduction observed with dapagliflozin vs. empagliflozin
Glycemic control	Reduction in fasting plasma glucose (up to -30.02 mg/dL)
	HbA1c reduction (-0.68%)
Weight management	Average weight reduction (-1.79 kg)
Lipid profile	Minimal impact on HDL; however, improvements in triglycerides in animal models
Renal protection	Reduction in uric acid levels (-1.03 mg/dL)
	Renoprotective effects, including reduced albuminuria
Anti-inflammatory effects	Reduction in inflammatory markers (e.g., IL-1β, IL-6)
Sympathetic nervous system	Modulation of SNS activity, reducing blood pressure and enhancing metabolic control

BP — blood pressure; IL — interleukin, HbA1c — glycated hemoglobin; HDL — high-density lipoprotein; SGLT2i — sodium-glucose cotransporter-2 inhibitors; SNS — sympathetic nervous system

Furthermore, there is a pressing need for targeted research into the etiology, epidemiology, and management of MetS, especially within the Indian context. Developing culturally tailored, evidence-based definitions and cut-off values for key parameters such as WC, waist-hip ratio, and fasting plasma glucose is essential for more accurate diagnosis and treatment of MetS in the Indian population. By prioritizing these public health measures and supporting them with focused research, we can substantially reduce the burden of MetS and its related health complications.

This structured approach, integrating both physical activity and dietary modifications, provides a comprehensive framework for the prevention and management of MetS, addressing both individual and community health needs.

Sodium-glucose cotransporter-2 inhibitors (SGLT2i) have emerged as a cornerstone in the battle against MetS, offering a comprehensive approach that addresses multiple aspects of this syndrome. SGLT2is, such as empagliflozin, dapagliflozin, and canagliflozin, have shown considerable promise in improving glycemic control, reducing body weight, lowering blood pressure, and decreasing uric acid levels. Beyond their glucose-lowering effects, these agents confer significant cardioprotective and renoprotective benefits, making them a powerful tool in the integrated management of MetS.

Table 4 summarizes the cardiometabolic benefits of SGLT2i, emphasizing their broad impact on various aspects of MetS and highlighting their role as a comprehensive treatment strategy.

The mechanisms by which SGLT2i exert their benefits are multifaceted. These agents reduce blood glucose levels by inhibiting glucose reabsorption in the renal proximal tubule, leading to glucosuria. This effect is independent of insulin and provides glycemic control even in patients with insulin resistance. Additionally, SGLT2is promote osmotic diuresis and natriuresis, contributing to reductions in plasma volume, blood pressure, and arterial stiffness. These effects not only improve metabolic parameters but also mitigate the risk of heart failure and other cardiovascular events [22].

Recent studies have also highlighted the anti-inflammatory properties of SGLT2is, which play a crucial role in reducing atherosclerosis and endothelial dysfunction — key drivers of CVD in MetS patients. By downregulating markers of inflammation, such as IL-1β, IL-6, and TNF-α, and improving lipid profiles, SGLT2is help to stabilize plaques and reduce the risk of adverse cardiovascular outcomes [23].

SGLT2is have been shown to modulate sympathetic nervous system (SNS) activity, which is often upregulated in patients with MetS and contributes to hypertension and insulin resistance. By reducing SNS activation, SGLT2is not only lower blood pressure but also enhance metabolic control, offering a dual benefit in managing both hypertension and insulin resistance [22, 24].

The comprehensive benefits of SGLT2is extend beyond the individual components of MetS, providing a holistic approach to managing this complex syndrome. As healthcare providers, it is imperative to embrace these therapeutic advancements and integrate them into our treatment strategies. Public health initiatives must also prioritize lifestyle modifications, such as promoting physical activity and healthy dietary habits, to prevent the onset of MetS. Early detection and intervention, particularly in high-risk populations, are crucial for curbing the global burden of this condition.

In conclusion, just as the Flag Satyagraha played a pivotal role in India's fight for independence, a modern Satyagraha against MetS can be instrumental in combating the escalating prevalence of this condition. By leveraging the full therapeutic potential of SGLT2i and fostering a culture of prevention and early intervention, we can make significant strides in improving public health outcomes and reducing the burden of chronic diseases associated with MetS.

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Author contributions

SSS: study design, literature search, intellectual content, manuscript preparation and review

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