Uttar Pradesh Association of Physicians of India Position Statement: Tobacco Use and Metabolic Syndrome

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Abstract

Tobacco use is one of the main preventable causes of mortality and morbidity worldwide. The global disease burden due to tobacco use is huge with projected mortality of eight million lives per year by 2030. Metabolic syndrome (MS) is defined as a constellation of cardiovascular and endocrine risk factors such as insulin resistance, obesity, raised blood pressure, and abnormal lipid profile. The relationship between tobacco use and MS has been well established. Also, the causal association between tobacco use and development of individual components of MS is well established.

The Uttar Pradesh Association of Physicians of India (UP API) has drafted this position statement on managing tobacco use among persons with or at risk of developing Metabolic Syndrome (MS). This position statement presents evidence-based recommendations as described below. Scope and purpose The objective of this position statement is to offer clinical recommendations for screening, diagnosis and management of tobacco use among persons with or at risk of developing Metabolic Syndrome (MS). The purpose of this document is to aid in identification and treatment of maladaptive patterns of tobacco use i.e. tobacco use disorder (tobacco dependence, harmful use, abuse) in person with or at risk of developing MS. Intended Audience The position statement is targeted at the clinicians engaged in care and management of person with or at risk of developing Metabolic Syndrome (MS). This might also be of relevance to the policy makers considering the public health burden of both MS and tobacco use disorders.

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Background

Tobacco use is one of the main preventable causes of mortality and morbidity worldwide. The global disease burden due to tobacco use is huge with projected mortality of eight million lives per year by 2030.1 Tobacco is used in both forms, smokable and smokeless, in India. Beedi, Cigarettes, Hooka, Chilam, Cigar, Churat are the smokable forms of tobacco. Smokeless forms of tobacco are consumed in chewable forms or snuff (through sniffing) or as a paste. Chewable forms of tobacco popularly used in India include Gutkha, Zarda, Khaini, Pan masala (with tobacco), Tobacco powder, Gul, Neswar, Mishri.2

The prevalence of tobacco use in India has been found to be 34.6%.3 In India, the prevalence of smokeless tobacco use (26%) was significantly higher than that of smoking (14%) and Khaini was the most common product used after beedi.3 As per the more recent National Family Health Survey 4, the prevalence of tobacco use among men and women aged between 15-49 years has been reported to be 57% and 10.8%, respectively. Contrary to the popular perception that smokeless forms are ‘safe’, smokeless form of tobacco is also an established risk factor for Cardiovascular Disease (CVD) and Metabolic Syndrome (MS), similar to smokable forms.4

Metabolic syndrome (MS) is defined as a constellation of cardiovascular and endocrine risk factors such as insulin resistance, obesity, raised blood pressure, and abnormal lipid profile.6 The relationship between tobacco use and MS has been well established. A greater body of evidence exists for association of smokable forms of tobacco and MS. The limited evidence on association between smokeless tobacco and MS could be a reflection of the limited attention given by the researchers to this tobacco form. In an Indian study, frequency of smokeless tobacco use (56%) was significantly higher than that of smokable tobacco (34%) in persons with MS.6

The causal association between tobacco use and development of individual components of MS is also well established.7 Decreased glucose uptake by skeletal muscle, increased leucocyte count, decreased adiponectin are some of the mechanisms postulated regarding the causation of MS by tobacco use.8 With tobacco use and MS being independent risk factors of CVD, the co-occurrence of tobacco use and MS is bound to add to the morbidity and mortality caused by these individually.

The Uttar Pradesh Association of Physicians of India (UP API) has drafted this position statement on managing tobacco use among persons with or at risk of developing Metabolic Syndrome (MS). This position statement presents evidence-based recommendations as described below.

Scope and purpose

The objective of this position statement is to offer clinical recommendations for screening, diagnosis and management of tobacco use among persons with or at risk of developing Metabolic Syndrome (MS). The purpose of this document is to aid in identification and treatment of maladaptive patterns of tobacco use i.e. tobacco use disorder (tobacco dependence, harmful use, abuse) in person with or at risk of developing MS.

Intended Audience

The position statement is targeted at the clinicians engaged in care and management of person with or at risk of developing Metabolic Syndrome (MS). This might also be of relevance to the policy makers considering the public health burden of both MS and tobacco use disorders.

Limitations

The position statement is based on evidence and has been written keeping in view the Indian context. However, due to paucity of exclusive literature on tobacco use among persons with MS, globally as well as from India, the recommendations have been extrapolated from literature on management of tobacco use disorders in general and in persons with Diabetes Mellitus (DM), Dyslipidemia and Hypertension as these form components of MS. The position statement should not be seen as a substitute to the standard clinical practice guidelines and it is advised to use this as a companion to the clinical practice and treatment guidelines.

Table 1: Evidence level used for rating various recommendations

<table>
<thead>
<tr>
<th>Evidence level</th>
<th>Evidence rating</th>
<th>Methodology</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Strong</td>
<td>Meta-analysis of randomized controlled trials</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Randomized controlled trials</td>
</tr>
<tr>
<td>2</td>
<td>Intermediate</td>
<td>Meta-analysis of non-randomized prospective or case-controlled trials, systemic literature review</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Non-randomized controlled trials</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Prospective cohort study</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Retrospective case-control study</td>
</tr>
<tr>
<td>3</td>
<td>Weak evidence</td>
<td>Cross-sectional study</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Surveillance study</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Consecutive case series</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Single case reports, observational study, pilot study</td>
</tr>
<tr>
<td>4</td>
<td>No evidence</td>
<td>Theory, opinion, consensus, review or pre-clinical study</td>
</tr>
</tbody>
</table>

Table 2: Grading of strength of recommendations

<table>
<thead>
<tr>
<th>Grade</th>
<th>Strength of recommendations</th>
</tr>
</thead>
<tbody>
<tr>
<td>A</td>
<td>Strong</td>
</tr>
<tr>
<td>B</td>
<td>Intermediate</td>
</tr>
<tr>
<td>C</td>
<td>Weak</td>
</tr>
<tr>
<td>D</td>
<td>Not evidence based</td>
</tr>
</tbody>
</table>
on management of tobacco use disorders.

**Grading of Evidence**

The current recommendations are graded based on the available evidence. The available evidence for individual recommendation is categorized in different levels as strong, intermediate, weak and no evidence. The strength of the recommendations is based on the level of evidence for the specific recommendation. The categories of the level of evidence and strength of recommendation given by American Association of Clinical Endocrinologists which has been previously employed for recommendations relevant to DM has been given in Tables 1 and 2, respectively. It must be noted that different evidence levels can be mapped to the same recommendation grade by ‘adjusting up’ or ‘adjusting down’ depending on the importance and relevance based on expert opinion.

**Clinically relevant issues related to tobacco use by persons with or at risk of developing Metabolic Syndrome (MS)**

- Tobacco use is not recommended in person with or at risk of developing MS as:
  - Smokable and smokeless forms of tobacco are known to increase insulin resistance and cause hyperinsulinemia. (3A)\(^{10}\)
  - Smokable and smokeless forms of tobacco are known to impair glycemic control and hasten development of complications of DM. (2A)\(^{11-13}\)
  - Smokable forms of tobacco are found to impair lipid profile by increasing Triglycerides (TG) and decreasing High Density Lipoprotein (HDL). (3A)\(^{14,15}\)
  - Smokable as well as smokeless forms of tobacco are known to increase waist hip ratio and cause obesity. (3A)\(^{16,17}\)
  - Smokable as well as smokeless forms of tobacco are known to increase systolic blood pressure. (3A)\(^{18-20}\)
  - Adverse impact of tobacco use in persons with or at risk of developing Metabolic Syndrome
    - Tobacco use is not recommended for persons at risk of developing MS as smoking has been found to be associated with development of MS. (1A)\(^{21}\)
    - Tobacco use is not recommended for persons at risk of developing DM as it accelerates development of DM in a dose dependent manner with reversal of effect on quitting. (2A)\(^{22}\)
  - Socio-Culturally acceptable substance use
    - Persons with or at risk of developing MS must be advised not to use tobacco in any form including hookah, betel quid (paan), gul, even if it is socio-culturally accepted. (3A)\(^{23}\)
  - Controversy of weight gain and increased risk of Metabolic Syndrome post tobacco cessation
    - Weight gain has been noted post tobacco cessation in the first year of abstinence and mainly in the first three months. (1A)\(^{24}\)
    - However, assessing the potential benefits of tobacco cessation such as increased insulin sensitivity despite the weight gain post cessation, tobacco cessation is recommended as the risk of MS is lower in smokers who have been abstinent compared to those who actively smoke and is higher compared to non-smokers. (3A)\(^{25}\)
  - In case post tobacco cessation weight gain is of concern the persons with or at risk of developing MS should be offered appropriate advise on diet and physical activity. (4A)
    - Pharmacokinetic and Pharmacodynamic interactions
      - Nicotine causes decreased insulin absorption as well as insulin resistance. (3A)\(^{26}\)
      - Nicotine through its sympathetic mediation decreases the action of beta blockers. Thereby, higher doses may be needed in smokers. (3A)\(^{27}\)
      - Post smoking cessation, antihypertensives and oral hypoglycemic agents metabolized by CYP1A2 need to be monitored. (3A)\(^{28}\)
  - The risk of metabolic syndrome exists with any kind of tobacco exposure such as direct smoke, smokeless and environmental exposure to tobacco smoke. Hence it is recommended that persons with or at risk of developing metabolic syndrome should not be exposed to any kind of tobacco. (3A)\(^{6,7,29}\)

**Screening for tobacco use (disorder) among persons with or at risk of developing Metabolic syndrome**

**General recommendations**

- Every person with or at risk of developing MS must be asked about tobacco use as a large scale study in India reported that only less than half of smokers and 27% patients using smokeless tobacco were asked to quit tobacco use by their physician. (3A)\(^{30}\)
- History about tobacco use must be elicited regarding reason of use, type, frequency, duration, time of first use once the person wakes up, usual dose and last dose. (4A)
- The person with tobacco use
must be asked about any other psychoactive substance use. (4A)

- The person with tobacco use must be asked regarding family or past history of psychiatric illness. (4A)

- Screening for tobacco use is highly recommended in the following clinical situations (4A):
  - Difficulty in controlling the use with increasing pattern of substance use compared to usual self.
  - Patients presenting with symptoms of withdrawal such as frustration, insomnia, irritability, anger, difficulty concentrating, restlessness, anxiety, decreased heart rate, increased appetite, dysphoric mood.31
  - Medical complications secondary to tobacco use.
  - Worsening glycemic profile with increasing trend of substance use.
  - Family history of psychiatric illness.
  - Past history of psychiatric illness.
  - Family history of substance use.
  - Family history of substance use.

Screening tools

- Screening tools used for assessing tobacco use (smokable) exclusively include Fagerström Test for Nicotine Dependence – Smokeless Tobacco (FTND ST), Tobacco Dependence Screener (TDS), Heaviness of ST use index (HSTI), ST dependence index (STDI), and ST quantity frequency index (ST-QFI). (3B)35
- It is recommended to prefer Fagerström Test for Nicotine Dependence (FTND) both smokable and smokeless tobacco in Indian setting as they have been validated in India. (3A)
- FTND is a six item questionnaire with maximum score of ten and score of equal to or more than five represents dependence. (3A)37,38
- ASSIST (Alcohol Smoking Substance involvement Screening Test) is recommended for screening for multiple psychoactive substances including tobacco. (2B)39
- ASSIST consists of eight questions assessing nine classes of substances over three month and life time periods and gives cut off scores for Brief Intervention and intensive intervention. (3A)39

Diagnosis of tobacco use disorder (dependence/harmful use) among persons with or at risk of developing MS

- Persons who screen positive for tobacco use are recommended to be further evaluated for dependence or harmful use. Diagnosis for dependence or harmful use can be established through the following criteria as laid by International Statistical Classification of Diseases and Related Health Conditions (ICD)-1040

- A diagnosis of harmful use refers to a pattern of psychoactive substance use that is causing damage to health i.e. either physical or mental harm
- A diagnosis of dependence can be made if three or more of the following criteria have been present over the previous 12 months-
  - Strong desire or sense of compulsion to take the substance
  - Difficulties in controlling substance-taking behaviour in terms of its onset, termination, or levels of use
  - A physiological withdrawal state when substance use has ceased or been reduced, as evidenced by: the characteristic withdrawal syndrome for the substance; or use of the same (or a closely related) substance with the intention of relieving or avoiding withdrawal symptoms
  - Evidence of tolerance, such that increased doses of the psychoactive substances are required in order to achieve effects originally produced by lower doses
  - Progressive neglect of alternative pleasures or interests because of psychoactive substance use, increased amount of time necessary to obtain or take the substance or to recover from its effects

### Table 3: Recommended interventions for tobacco use based on score on screening instrument ASSIST39

<table>
<thead>
<tr>
<th>Instrument</th>
<th>Score/risk level for tobacco use</th>
<th>Recommended intervention</th>
</tr>
</thead>
<tbody>
<tr>
<td>ASSIST</td>
<td>Lower risk (0-3)</td>
<td>General health advice</td>
</tr>
<tr>
<td></td>
<td>Moderate (4-26)</td>
<td>Brief intervention</td>
</tr>
<tr>
<td></td>
<td>High (&gt; 26)</td>
<td>Brief intervention; Referral to specialist for assessment and treatment</td>
</tr>
</tbody>
</table>

- Screening tools used for assessing tobacco use (smokable) exclusively include Fagerström Tolerance Questionnaire (FTQ), Fagerström Test for Nicotine Dependence (FTND), Tobacco Dependence Screener (TDS). (2A)32-34
Persisting with substance use despite clear evidence of overtly harmful consequences

Treatment of tobacco use disorder among persons with or at risk of developing MS

- Integrated management of tobacco use disorder among persons with or at risk of developing MS is recommended. (4A)
- A combination of pharmacological and non-pharmacological interventions is recommended.41 (1A)
- The quality of evidence is low regarding electronic cigarette in cessation of smoking and its use is not recommended. (1A)42

Non-pharmacological treatment

- Anti-craving measures in form of stimulus control which is reducing exposure to stimulus, coping imagery, `urge surfing` incorporating 5 ‘D’ approach may be recommended to the persons with tobacco use. (3B)43 The 5 ‘D’ includes:
  - Delay the urge
  - Distract yourself
  - Drink water
  - Deep breathing
  - Discuss with someone
- For tobacco users who are willing to quit, tobacco cessation counseling in form of 5 ‘A’ approach is recommended (3B).44,45 The 5 ‘A’ approach includes:
  - Ask about tobacco use at each visit
  - Advise to quit
  - Assess willingness to quit
  - Assist in quitting
  - Arrange for follow up
- For tobacco users who are not willing to quit, 5 ‘R’ approach is recommended (3B).44,45 The 5 ‘R’ approach includes:
  - Relevance of quitting tobacco to the patient
  - Risks of tobacco use
  - Rewards of tobacco cessation
  - Roadblocks to quit
  - Repetition of the message to quit
- Evidence-based psychosocial interventions include Brief Interventions, Cognitive Behavioral Therapy (CBT) including Relapse Prevention (RP), Motivational Enhancement/Motivational Interviewing (MI), Contingency Management (CM) 46,47
- Brief Intervention (BI) is recommended for persons with tobacco use, specially in primary care setting, with low level of dependence and in adolescents.48,49 (3A) FRAMES is an acronym for the components of BI as described below:
  - F- Feedback
  - R- Responsibility
  - A- Advice
  - M- Menu of options
  - E- Express Empathy
  - S- Support self efficacy
- The main component of CBT is assessing cognitive distortions that are dysfunctional beliefs about tobacco use and evaluating “apparently irrelevant decisions” leading to relapse. Relapse Prevention (RP) is an essential component of CBT. Owing to time constraints, the busy physician may not be able to use all the strategies of RP. It is advisable to offer RP under the guidance of qualified mental health professional, especially when the physician is new to this intervention.50 It is possible to train the paramedical staff and nurses in delivery of Brief Interventions.
- Non-pharmacological management of tobacco use based on score of ASSIST - Score on a screening scale like ASSIST can be used to identify the appropriate type of intervention for tobacco use.

Lifestyle modifications

- Lifestyle modifications comprising of dietary changes and appropriate physical activity is recommended and must be advised.(1B)51

Psycho-education

- Psychoeducation for tobacco use among persons with or at risk of developing MS must include the following components.(4A):
  - The combined deleterious effect of tobacco use and MS
  - Tobacco use, even though socially acceptable, is not a simple behavioral change and problematic tobacco use patterns such as dependence/ harmful use needs treatment
  - Even if the pattern of tobacco use is not qualifying for tobacco use disorder, the patient must be advised to abstain from tobacco use
  - Dietary modification and appropriate physical activity must be advised

Pharmaceutical management of nicotine dependence

- Nicotine Replacement Therapy (NRT), Bupropion, Varenicline, Cystine, Nortryptiline have evidence base for management of tobacco use disorders.52
- NRT is recommended for increasing the rate of quitting, as it shows 50 to 70% efficacy across multiple setting. (1A)53,54
- Though older evidence reports that inhaled nicotine is better than other forms, recent evidence suggests that there is no difference of efficacy among the forms.54,55
- In the Indian setting, Nicotine Patch or Nicotine gums or lozenges are recommended due to availability, affordability
and accessibility.54 (4A)

- NRT has been found to work irrespective of the patient receiving any non-pharmacological management.54 (1B)

- The chances of abstinence are found to increase when started before the ‘quit date’.54 (1A)

- The chances of abstinence are higher with combination of NRT compared with single form of NRT alone.54 (1B)

- In persons with high level of dependence it is recommended to prescribe 4mg nicotine gum.54 (1A)

- Weaker evidence exists regarding higher doses of Nicotine patch in cases of high level of tobacco dependence.54 (1A)

- High level of evidence exists for Bupropion as single agent for long term tobacco cessation.56 (1B)

- Moderate level of evidence exists for Nortriptyline as single agent for long term tobacco cessation.56 (1B)

- Combination of Bupropion or Nortriptyline with NRT is not recommended as no additional benefit was observed with combination compared to either of the two alone.56 (1B)

- High quality of evidence exists for Varenicline being significantly better compared to Bupropion.57 (1B)

- Moderate quality of evidence exists for Varenicline being significantly better compared to NRT.57 (1B)

- Cystine is not recommended currently due to modest evidence of its efficacy.57 (1B)

- Clonidine is not recommended due to modest effect size as well as due to side effect profile.58 (1A)

- NRT, sustained release Bupropion and Varenicline are recommended as first-line agents.59 (1B)

Active monitoring and follow up

- Persons with or at risk of developing MS must be systematically asked for tobacco use at the follow-up. (4A)60

- Those who are not able to abstain despite being compliant to the treatment may, at times, have psychiatric comorbidity and thereby may warrant referral to psychiatrist for further evaluation. (4A)60

- Though recent studies report absence of any significant neuropsychiatric adverse effects with Bupropion or Varenicline, patients must be asked regarding suicidal ideation and evaluated for emergence of any adverse effects including neuropsychiatric adverse effects. (1B)61

Referrals for tobacco use among persons with or at risk of developing MS

- Referral form must include reason for referral along with socio-demographic and clinical profile of the patient as well as details of the treatment given both for MS as well as for tobacco use. (4A)60

- Persons unable to remain compliant or unable to tolerate adverse effects of medication may need referral to psychiatrist. (4A)60

- Persons with past or family history of psychiatric illness or suicidal ideation needs referral to mental health professional. (4A)60

- Persons who need structured psychosocial interventions such as CBT/MI/CM should be referred to mental health professional. (4A)60

- Special population such as pediatric and geriatric age group patients and pregnant women may need evaluation by psychiatrist. (4B)60

References


46. Miller WR, Sanchez VC. Marketing tobacco/nicotine to children, adolescents, and young adults: evidence from youth and young adult surveys. JAMA 2006; 295:1176–82.
