Journal of Cardiovascular Disease Research

ISSN: 0975-3583,0976-2833 VOL13, ISSUE 05, 2022

Original Article

PREVALENCE AND PROGRESSION OF METABOLIC SYNDROME IN PATIENTS OF DEPRESSION

SK Samal[1], NeelamRathi[1], Sanjay Kumar[2], PreetiPatni[3]

[1]Associate Prof -Psychiatrist at Military HospMeerut, Uttar Pradesh,India
[2]Associate Prof - Psychiatrist at Command Hosp, Chandimandir, India,
[3]Prof - Pathologist at Military Hosp Jalandhar, Punjab, India

Corresponding Author-Dr NeelamRathi
Email: drneelamrathi@gmail.com

Source of support: None, **Conflict of interest**: None

ABSTRACT

Objective: To assess prevalence and progression of Metabolic Syndrome (MetS) in patients of depression and effects of antidepressants in development of Metabolic Syndrome (MetS).

Materials and Method: This longitudinal study was conducted in a tertiary care hospital of India between Jun 2015 to Jun 2018. Data was collected during six months follow up of patients at psychiatric OPD.

Results: 13.87% of screened population had depressive illness. 21.4% achieved complete remission in 6 months.MetS increased from 14.83%to29.04% in 6 months (p=0.003). Central obesity increased from 19.91%to34% (p=0.008).

Discussion and Conclusions: Prevalence of MetS in consenting patients treated for clinical depression with pharmacotherapy was14.83%. Rising figure of MetS prevalence to 29.04% at 6 months follow up depicts a clear role of antidepressant medication in development of MetS.Central obesity during six-month follow up increased from 19.91% to 34%.

Keywords- Metabolic Syndrome, Depression, Antidepressant medication

INTRODUCTION

METABOLIC SYNDROME: THE ENTITY Description of clustering metabolic abnormalities has evolved across last century since initial mention in 1923 by Swedish Physician EskilKylin(1). Conglomeration of metabolic abnormalities has been named by a plethora ofvocabulary in last few decades including Syndrome X by Reaven in 1988 and subsequently various scientific bodies have come up with terms like Insulin Resistance Syndrome as well asMetabolic Syndrome(MetS)(2).Research indicatesinterplay of adipocyte macrophages, hormones and epigenetic phenomenon(3).This entity was defined by WHO as a pathologic condition characterized by abdominal obesity, insulin resistance, hypertension and hyperlipidaemia. Global consensus was achieved with the term Metabolic Syndrome defined by gender and race specific central adiposity indicated by waist circumference (WC) and two of the others in the IDF criteria (4, 5):

ISSN: 0975-3583,0976-2833 VOL13, ISSUE 05, 2022

A. Waist circumference: for Indians; male>94 cms, female>80 cms
B. Raised triglycerides: Fasting >150 mg/dL or specific medication
C. Gender-wise HDL levels or specific medication:
   (i) Men <40 mg/dL
   (ii) Women <50 mg/dL
D. Hypertension: Raised BP or previous diagnosis or specific medication
   (i) Systolic >130 mm Hg
   (ii) Diastolic >85 mm Hg
E. Fasting plasma glucose >100 mg/dL or previous diagnosis of Type 2 Diabetes

METABOLIC SYNDROME: BIOLOGY AND STATISTICS: Although prevalence of MetSvaries across races,It'srise with age is well documented. In India, prevalence among men and women are estimated about 33.3% and 40.4% respectively (6, 7). Prevalence of MetS is increasing worldwide, as high as 49.1% (8). For the adult population it is estimated to be range from 20 to 25%(5). A pooled analysis of previous literature concluded a global prevalence of 7% as per the IDF criteria above in relativelyyounger age group 18-30 years. Among components of MetS, low HDL was 26.9 to 41.2% as the most prevalent and excess fasting plasma glucose was as low as 2.8 to 15.4% to be the least prevalent. Other components like raised BP ranged from 16.6 to 26.6%, central adiposity 6.8 to 23.6% and fasting TG 8.6 to 15.6% respectively(9).Understanding biology of this malady is also taking new turns with modern research. Activating brown adipocytes by various mechanisms isforeseen as a potential therapeutic measure targetingMetS(10). About three decades after discovery of leptin adipose tissue has been established as an endocrine organ. Through bioactive molecules including hormones now termed as adipokines, adipose tissue influences the regulation of several important physiological functions including appetite, satiety, energy expenditure, activity level, insulin-related functions of sensitivity and secretion, glucose and lipid metabolism, fat distribution, endothelial function, haemostasis, blood pressure, neuroendocrine regulation and function of the immune system(11). Abdominal obesity (AO) has been found as uniquely related to decreased plasma concentrations of adiponectin and increased leptin levels. AO also gets associated with a decreased vascular response to acetylcholine and an increased vasoconstriction in response to angiotensin II (Ang II) (12). Role of inflammatory cytokines is also opening new areas of research. Among recent developments, Oncostatin-M (OSM), a member of the IL-6 family holds promise in prevention of late-onset MetS in the genetically vulnerable following encouraging results involving mice (13).Depression and MetS have been proven to have a bidirectional causal relationship (14).Irrespective of gender, people with metabolic syndrome are more likely to have depressive symptoms as compared to their healthy counterparts (15).

METABOLIC SYNDROME AND DEPRESSION In depression, activation of hypothalamo-pituitary-adrenal(HPA)axis,increasedhydro-corticotrophin,adrenocorticotropic and cortisol hormones releasesignificantly facilitate deposition of visceral adipose tissue(16).The syndrome of depression also clusters symptoms like poor dietary intake, diet quality and reduced physical activity(17).Antidepressants, especially tricyclic antidepressantsmay also result in causation of MetS(18, 19). Furthermore, atypical depression

ISSN: 0975-3583,0976-2833 VOL13, ISSUE 05, 2022

involves excessive eating that has risk of MetS(20). Depression also has been linked to aetiology involving pro-inflammatory states(21-23). It also has been postulated that MDD and MetS share metabolic, immune-inflammatory, oxidative and nitrosative stress pathways (24). Some researchers link maladaptive lifestyle factors like drinking and smoking to causation of MetS in patients of major depression (25).In patients with depressive disorders, prevalence of MetS varies from 25% to 48.1% in different studies (19).In neuro-imaging, reduced globuspallidius volume, a basal ganglia component was correlated toMetS and depressive symptoms(26).Depressive illnesses correlate to approximately two-fold increased risk of the MetS(27). Effect of MetS on time to remission in depression remains inconclusive (28, 29).

NEED FOR THIS RESEARCH: In industrial populations, prevalence of MetS at the time of diagnosis of Depression remains a less explored entity. Depression among troops significantly affects the fighting ability of individual, requiring specific measures.unit's productivity also gets affected due to this morbidity. Caring for the combatants suffering from depression becomes a concern since they require significant time to recover. MetS affecting the outcome of depression in this population also needs to be ascertained. Also, there is a need to study whether holistic treatment of depression improves MetS in the long run or not.

REVIEW OF LITERATURE

In a meta-analysis and systematic review of literature, Ghanei et al. concluded that in five statistically significant studies, based on odds ratio, the risk of MetS is 1.5 times higher in depressed patients than in non-depressed patients and the significance was more in cross-sectional studies (25). Marazziti et al concluded that there is a four-fold risk of premature death in major depression largely accounted by cardiovascular diseases most likely mediated by MetS and highlighted MetS as the hallmark of unhealthy lifestyle in patients with depression (30).Moradi et al concluded from meta-analysis of cohort studies that depressed men are more likely to develop MetS than depressed women apart from identifying factors of unhealthy lifestyle, poor treatment adherence(31). As per van ReedtDortland et al, symptom severity with antidepressant medication were positively associated with MetS and specifically linked TCA to MetS(32).Bekhbat et al demonstrated a single infusion of TNF antagonist Infliximab reduced cholesterol in depressed patients with high CRP compared to placebo with consistent finding of high inflammation in patients of depression being associated with metabolic alterations with CRP>5 mg/L at baseline (33).Among Indian studies, prevalence of depression among urban South Indians was 15.1% with age adjusted population based higher occurrences in females, low income group and divorced as well as widowed (34). As per Agarwal et al, presence of central obesity was significantly higher in recurrent depression (30%) and bipolar depression (24%) as compared to controls (8%) (35).

ISSN: 0975-3583,0976-2833 VOL13, ISSUE 05, 2022

AIM AND OBJECTIVES

The aim of the study was to evaluate the prevalence and progression of MetS in patients with Depression in industrial population.The study made an attempt to achieve following objectives considering the industrial population. Two primary objectives were aimed at to be fulfilled. In addition, following secondary objectives were also measured.

PRIMARY OBJECTIVES:

(a) To assess prevalence of MetS in patients of Depression

(b) To assess the effects of antidepressants in development of MetS in these patients

SECONDARY OBJECTIVES:

(a) To assess prevalence of depression in industrialpopulation

(b) To measureincidence of Central Obesityduring antidepressant treatment

MATERIALS AND METHOD

Thislongitudinalstudy was conducted in a tertiary care service hospital on an industrial population which included the resident service population and families in the station with established healthcare infrastructure.

The study was conducted for a period of three years on patients withsyndromaldepression under follow up from service hospital. Six-month follow up data was collected during monthly visits at psychiatric OPD. To measure population prevalence of depression and MetS, periodic screening was conducted separately. Data was collected from Jun 2015 to Jun 2018.

The study obtained permission from the institutional ethical committee. All subjects gave informed consent.

INCLUSION CRITERIA The following inclusion criteria were followed:

A. Consenting patients in the industrial population
B. Age group 18-56

EXCLUSION CRITERIA The following exclusion criteria were followed:

A. Unwilling patients
B. Moribund patients
C. Patients of Bipolar Affective Disorder and Schizoaffective Disorder

VARIABLES The following variables were studied during this research.

A. Psychosocial proforma containing patient details
B. Biometric parameters:
    -Waist circumference
    -Height
    -Weight
    -BMI
C. Laboratory parameters
    -HDL
    -Triglycerides
    -Blood Sugar: Fasting and Post Prandial

ISSN: 0975-3583,0976-2833 VOL13, ISSUE 05, 2022

METHODOLOGY

A total of 4967 volunteersfrom age group of 18 to 56 yrs&without any known psychiatric ailments were screened in population-based programmes using clinical toolsduringJun 2015 to Jun 2018 for the study.History of any disease and past or present medication was recorded. After getting a duly signed informed consent from the participants were given a booklet in Englishcontaining a specially made psychosocial proforma and questionnaire for psychometric tool. Wide range of data was collected. Involving pharmacotherapy and psychotherapy, the study was conducted in following steps:

A. Screening of the populationwas done in various segments of the industrial population for prevalence of depression.Various public outreach programmes were utilized during lectures by Psychiatrist, Family Counsellors, Clinical Psychologists and psychiatric nurses. It is to be noteworthy that the place had a robust infrastructure for the workers as well as family members in form of Psychiatric Rapid Intervention Team and Mental Health Organization. Apart from that, various community day programmes organized were targeted for screening. With a cut-off of 7 in depression subscale, Hospital Anxiety and Depression Scale (HADS) was used(36).

B. Longitudinal follow-up for depression:Subjects were selected in the longitudinal follow-up study on basis of voluntary participation and presence of clinical depression. Although 689 subjects scored above cut-off for depression subscale in HADS, 344 met with criteria for a clinical diagnosis. 284 subjects consented to participate in longitudinal follow-up. After establishment of a clinical diagnosis, they were rated by a more definitive rating scale for this follow up. Hamilton Depression Rating Scale HAM ‘D’ was used for the same considering its reputation as a gold standard in rating the illness(37,38). The subjects were thoroughly assessed for severity of depression by HAM ‘D’ and presence of metabolic syndrome at six monthly intervals. A cut-off of 7 was taken for complete remission (39).Only 271subjects were available after 6 months as 13 patients had dropped out.

(i) Central Obesity: Anthropometric measure of waist circumference was taken. Gender-wise cut-offs of 94cms and 88cms were used for males and females respectively.

(ii) Hypertension: The population was screened with cut-offs of 130 and 85 mm Hg for systolic and diastolic blood pressure respectively.

(iii) Hyperglycaemia: Fasting plasma sugar of 100 mg/dL was cut-off.

(iv) Hypertriglyceridemia: Fasting sample cut-off was 150 mg/dL.

(v) Low HDL cholesterol: Gender-wise cut-offs were 40 mg/dL and 50 mg/dl for males and females respectively.

RESULTS

SCREENING FOR DEPRESSION AND FOLLOW UP THEREOF- Out of4967 volunteers screened using Hospital Anxiety and Depression Scalewith clinical cut-off of 7 in depression subscale. 689 people scored above cut-off for depression subscale.

13.87% of screened population had depressive illness (Fig 1)

ISSN: 0975-3583,0976-2833 VOL13, ISSUE 05, 2022

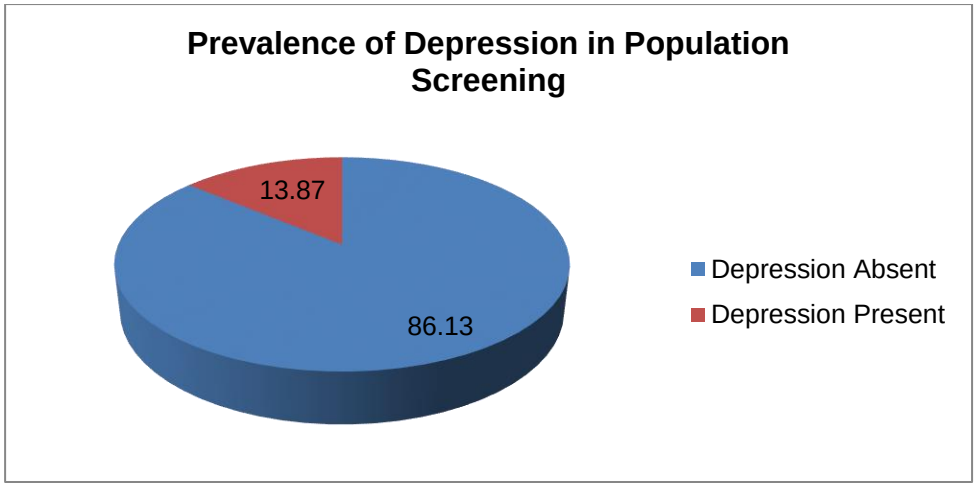


Figure 1: Prevalence of Depression in Population Screening

At 6-month follow-up, 58 out of 271 subjects (21.4%) achieved complete remission (p~0).

PREVALENCE OF METABOLIC SYNDROME IN PATIENTS OF DEPRESSION

After considering the number of patients present at 6-month follow-up, a prevalence rate of 14.83% was noted for MetSas per IDF criteria(Fig 2).

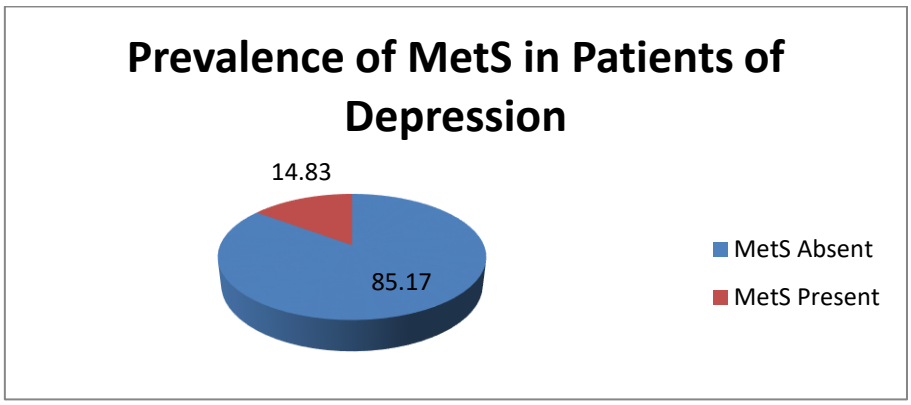
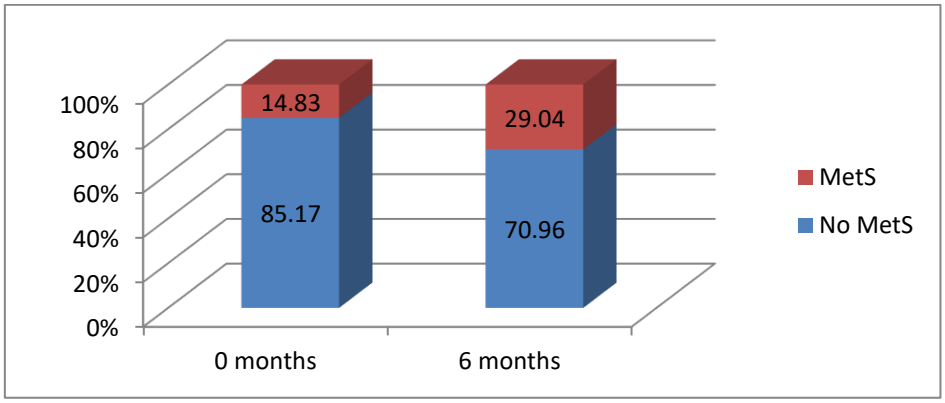


Figure 2: Prevalence of MetS in Patients of Depression

During 6-month follow-up, MetS increased from 14.83%t0 29.04%, had(p=0.003) (Fig-3)



ISSN: 0975-3583,0976-2833 VOL13, ISSUE 05, 2022

Figure 3: MetS in Patients of Depression at 6 Months Follow-up (p=0.003)

CENTRAL OBESITY **:** After considering the number of patients present at 6-month follow-up, a prevalence rate of 19.91% was noted for Central Obesityas per IDF criteria(Fig-4).

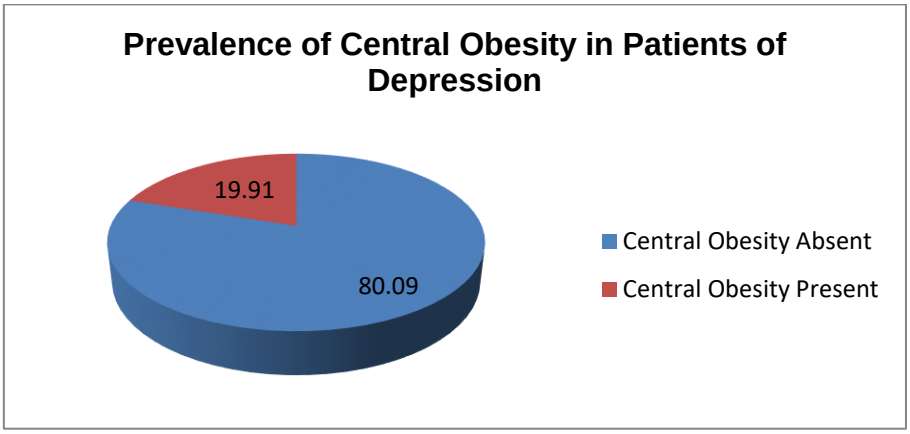


Figure 4: Prevalence of Central Obesity in Patients of Depression

During 6-month follow-up, central obesity increased from 19.91%to34% (p=0.008)(Fig-5).

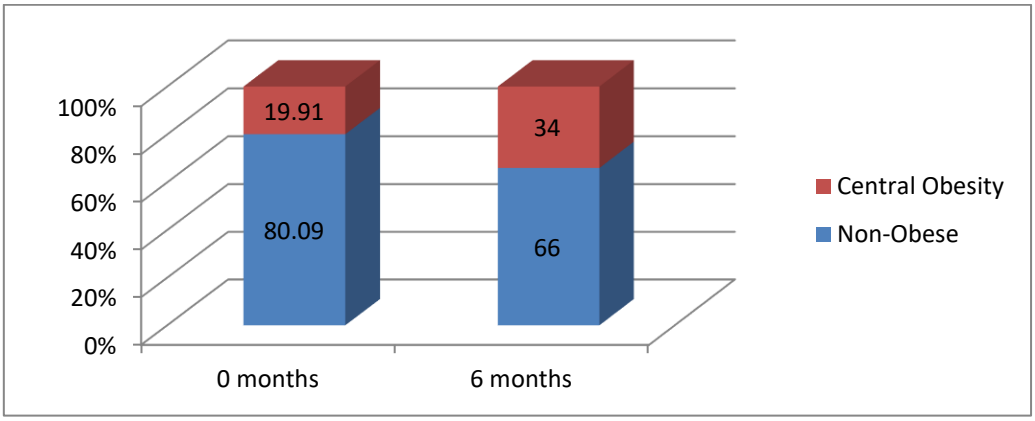


Figure 5: Central Obesity in Patients of Depression at 6 Months Follow-up (p=0.008)

The remaining data regarding contribution of blood pressure, triglyceride, HDL and blood sugar were not statistically significant in the study. This indicates further study on the matter with a larger sample size since various studies in existing literature have put light on these factors becoming significant.

DISCUSSION

METABOLIC SYNDROME IN PATIENTS OF DEPRESSION The prevalence of MetS in consenting patients treated for clinical depression with pharmacotherapy was 14.83%. Since the study population was not a closed group and during data analysis the number of entrant participants varied in 6-monthssince several populations either migrated or remitted

ISSN: 0975-3583,0976-2833 VOL13, ISSUE 05, 2022

completely, the prevalence was taken as 14.83% for the follow up.A study by Nebhinani et al on prevalence of MetS in drug-naïve patients with depression gives a figure of 27.7% (40). The lower prevalence rate may be a characteristic of study population that largely takes measures for early detection, treatment and preventive measures.

EFFECT OF ANTIDEPRESSANT MEDICATIONS IN DEVELOPMENT OF METABOLIC SYNDROME The fact to be emphasized upon is that all the treated patients were given antidepressants as per the design of the study. Rising figures of MetSprevalence from 14.83% to 29.04% at 6 months follow up depicts a clear role of antidepressant medication in development of MetS.Increasing incidence in MetS during the process of treatment with antidepressants may however be multi-factorial. Physical inactivity in course of the syndromal illness, attainment of chronicity in some, pharmacotherapy and other lifestyle factors like diet and some mal-adaptive habits like smoking and drinking may be key contributors. Central obesity being the factor in MetS with maximum weightage; requires due attention in form of lifestyle modification, increasing physical activity and diet planning etc. This comes in line with an Indian study on depressed patients where MetS in depressive disorders was 44.3% against a healthy control group (17.3%) as concluded by Grover et al. (41). This largely comes in line with the existing literature as longer course of the illness has to play with biological factors of inflammation and effects of anti-depressants. However, no data was available on antidepressant class on causation of MetS.Also, adjunct antipsychotic and mood stabilizer data was not taken.

PREVALENCE OF DEPRESSION IN REFERENCE POPULATION:

Thepopulation under study included working as well as their family members. The family members constituted the bigger contributor to the study population. A significant percentage of industrialpopulation has depressive illness 13.87%. The value is little less than the Indian prevalence of depression among urban population discussed earlier. As far as severity of depression goes, the study did not aim at the factor. Although all of them do not seek psychiatric treatment, but they definitely require supportive services like that of Psychologist, Family Counsellor and Psycho-Social Worker. It is noteworthy that in depression that is of recent onset and mild in severity; the modalities of management include active monitoring, individual-guided self-help, CBT and exercise. DSM 5 data on 12-month and lifetime prevalence of major depression was 10.4% 20.6% in USA respectively(42). The difference from reference studies may be explained by population characteristic, tool used and with the method of data collection which was purely self-reported and no clinical interview was conducted till that point of study.

INCIDENCE OF CENTRAL OBESITY DURING ANTIDEPRESSANT TREATMENT

The finding of central obesity 19.91% during entry point of study that increased up to 34% at 6 months largely falls in line with the Indian studies. This statistically significant component of MetS emphasizes on various preventive measures of lifestyle modification in patients of depression moving towards a chronic course.

ISSN: 0975-3583,0976-2833 VOL13, ISSUE 05, 2022

REMMISSION RATES FOR DEPRESSION TREATMENT The figures of 21.4% for remission at 6 months depicts need for a significant time period for follow up to improve efficacy of treatment in real-world scenario.

CONCLUSION

On the basis of above statistically significant findings, following conclusions are made:

SCREENING PATIENTS OF DEPRESSION FOR EARLY IDENTIFICATION FOR METABOLIC SYNDROME Treatment of depression requires a long time to achieve remission in real world scenario. Cases attaining chronicity are at high risk to develop MetS. Promoting healthy lifestyle like physical exercise, healthy diet, zero use of intoxicants can be ensured by regular follow up. Psychiatric services should include regular assessment of all the metrics of MetS periodically. Identifying risk factors like physical inactivity, unhealthy dietary habit use of alcohol, tobacco and other intoxicants and other maladaptive habits and necessary preventive measures can be taken in patients coming for regular follow up.

PROVISIONING OF SERVICES Professional services like that of dietician, physical trainers, psychologist, family counsellor, psycho-social workers are of paramount significance during follow up of depression which may start at screening of the population. A population-based outreach strategy will definitely improve outcomes in respect to Depression as well as MetS.

INFRASTRUCTRE EXPANSION Infrastructure for medical services including psychiatric services hold key to effective follow up.At the same time infrastructures for healthy lifestyle like sports facilities, swimming pools, gymnasiums and walking plaza etc. also are key to promote health as well as prevent MetS.

STRENGTH OF THE STUDY:

(a) The longitudinal study was conducted on real-world scenario.
(b) Risk of patients of depression to develop MetSwas elicited.
(c) Strict criteria were duly followed for depression and MetS.
(d) Most of the study cohort was regular in follow up.
(e) The study opens up horizon for modern interventional studies.

LIMITATIONS:

(a) Role of individual pharmacological agents to develop MetSwas not taken into consideration.
(b) Duration of depressive illness at entry to study wasn’t elicited.
(c) Subjects lost to follow up were not classified to remitted and migrated adequately
(d) Treatment data of metabolic disorder was not available.

ISSN: 0975-3583,0976-2833 VOL13, ISSUE 05, 2022

BIBLIOGRAPHY

1. Nilsson S. [Research contributions of Eskil Kylin]. Svensk medicinhistorisk tidskrift. 2001;5(1):15-28.
2. Parikh RM, Mohan V. Changing definitions of metabolic syndrome. Indian Journal of Endocrinology and Metabolism. 2012;16(1):7-12.
3. Saklayen MG. The Global Epidemic of the Metabolic Syndrome. Current hypertension reports. 2018;20(2):12.
4. Alberti KGMM, Zimmet P, Shaw J. Metabolic syndrome—a new world-wide definition. A Consensus Statement from the International Diabetes Federation. Diabetic Medicine. 2006;23(5):469-80.
5. Information on the IDF consensus worldwide definition of the metabolic syndrome. Available: http://www.idf.org/webdata/docs/IDF_Meta_def_final.pdf. : International Diabetes Federation [Accessd 23 Sep 2018].
6. Grover S, Nebhinani N, Chakrabarti S, Avasthi A, Kulhara P, Basu D, et al. Comparative study of prevalence of metabolic syndrome in bipolar disorder and schizophrenia from North India. Nordic journal of psychiatry. 2014;68(1):72-7.
7. Misra A, Shrivastava U. Obesity and Dyslipidemia in South Asians. Nutrients. 2013;5(7):2708-33.
8. Raposo L, Severo M, Barros H, Santos AC. The prevalence of the metabolic syndrome in Portugal: the PORMETS study. BMC public health. 2017;17(1):555.
9. Nolan PB, Carrick-Ranson G, Stinear JW, Reading SA, Dalleck LC. Prevalence of metabolic syndrome and metabolic syndrome components in young adults: A pooled analysis()(). Preventive Medicine Reports. 2017;7:211-5.
10. Sun L, Camps SG, Goh HJ, Govindharajulu P, Schaefferkoetter JD, Townsend DW, et al. Capsinoids activate brown adipose tissue (BAT) with increased energy expenditure associated with subthreshold 18-fluorine fluorodeoxyglucose uptake in BAT-positive humans confirmed by positron emission tomography scan. The American journal of clinical nutrition. 2018;107(1):62-70.
11. Bluher M, Mantzoros CS. From leptin to other adipokines in health and disease: facts and expectations at the beginning of the 21st century. Metabolism: clinical and experimental. 2015;64(1):131-45.
12. Lopez-Jaramillo P, Gomez-Arbelaez D, Lopez-Lopez J, Lopez-Lopez C, Martinez-Ortega J, Gomez-Rodriguez A, et al. The role of leptin/adiponectin ratio in metabolic syndrome and diabetes. Hormone molecular biology and clinical investigation. 2014;18(1):37-45.
13. Komori T, Morikawa Y. Oncostatin M in the development of metabolic syndrome and its potential as a novel therapeutic target. Anatomical science international. 2018;93(2):169-76.
14. Ghanei Gheshlagh R, Parizad N, Sayehmiri K. The Relationship Between Depression and Metabolic Syndrome: Systematic Review and Meta-Analysis Study. Iranian Red Crescent Medical Journal. 2016;18(6):e26523.
15. Koponen H, Jokelainen J, Keinanen-Kiukaanniemi S, Kumpusalo E, Vanhala M. Metabolic syndrome predisposes to depressive symptoms: a population-based 7-year follow-up study. The Journal of clinical psychiatry. 2008;69(2):178-82.

ISSN: 0975-3583,0976-2833 VOL13, ISSUE 05, 2022

16. Dunbar JA, Reddy P, Davis-Lameloise N, Philpot B, Laatikainen T, Kilkkinen A, et al. Depression: an important comorbidity with metabolic syndrome in a general population. Diabetes care. 2008;31(12):2368-73.
17. Kaner G, Soylu M, Yüksel N, Inanç N, Ongan D, Başmısırlı E. Evaluation of Nutritional Status of Patients with Depression. Biomed Res Int. 2015;2015:521481-.
18. Pan A, Keum N, Okereke OI, Sun Q, Kivimaki M, Rubin RR, et al. Bidirectional association between depression and metabolic syndrome: a systematic review and meta-analysis of epidemiological studies. Diabetes care. 2012;35(5):1171-80.
19. Kozumplik O, Uzun S. Metabolic syndrome in patients with depressive disorder--features of comorbidity. Psychiatria Danubina. 2011;23(1):84-8.
20. Blanco C, Vesga-Lopez O, Stewart JW, Liu SM, Grant BF, Hasin DS. Epidemiology of major depression with atypical features: results from the National Epidemiologic Survey on Alcohol and Related Conditions (NESARC). The Journal of clinical psychiatry. 2012;73(2):224-32.
21. Young JJ, Bruno D, Pomara N. A review of the relationship between proinflammatory cytokines and major depressive disorder. Journal of affective disorders. 2014;169:15-20.
22. Kim YK, Na KS, Myint AM, Leonard BE. The role of pro-inflammatory cytokines in neuroinflammation, neurogenesis and the neuroendocrine system in major depression. Progress in neuro-psychopharmacology & biological psychiatry. 2016;64:277-84.
23. Himmerich H, Patsalos O, Lichtblau N, Ibrahim MAA, Dalton B. Cytokine Research in Depression: Principles, Challenges, and Open Questions. Frontiers in Psychiatry. 2019;10(30).
24. de Melo LGP, Nunes SOV, Anderson G, Vargas HO, Barbosa DS, Galecki P, et al. Shared metabolic and immune-inflammatory, oxidative and nitrosative stress pathways in the metabolic syndrome and mood disorders. Progress in neuro-psychopharmacology & biological psychiatry. 2017;78:34-50.
25. Ghanei Gheshlagh R, Parizad N, Sayehmiri K. The Relationship Between Depression and Metabolic Syndrome: Systematic Review and Meta-Analysis Study. Iran Red Crescent Med J. 2016;18(6):e26523.
26. Onyewuenyi IC, Muldoon MF, Christie IC, Erickson KI, Gianaros PJ. Basal ganglia morphology links the metabolic syndrome and depressive symptoms. Physiology & behavior. 2014;123:214-22.
27. Foley DL, Morley KI, Madden PAF, Heath AC, Whitfield JB, Martin NG. Major depression and the metabolic syndrome. Twin Res Hum Genet. 2010;13(4):347-58.
28. Mulvahill JS, Nicol GE, Dixon D, Lenze EJ, Karp JF, Reynolds CF, 3rd, et al. Effect of Metabolic Syndrome on Late-Life Depression: Associations with Disease Severity and Treatment Resistance. Journal of the American Geriatrics Society. 2017;65(12):2651-8.
29. Ruas LG, Diniz BS, Firmo JO, Peixoto SV, Mambrini JV, Loyola-Filho AI, et al. Components of the metabolic syndrome and depressive symptoms in community-dwelling older people: the Bambui Cohort Aging Study. Revista brasileira de psiquiatria (Sao Paulo, Brazil : 1999). 2016;38(3):183-9.
30. Marazziti D, Rutigliano G, Baroni S, Landi P, Dell'Osso L. Metabolic syndrome and major depression. CNS spectrums. 2014;19(4):293-304.

ISSN: 0975-3583,0976-2833 VOL13, ISSUE 05, 2022

31. Moradi Y, Albatineh AN, Mahmoodi H, Gheshlagh RG. The relationship between depression and risk of metabolic syndrome: a meta-analysis of observational studies. Clinical Diabetes and Endocrinology. 2021;7(1):4.
32. van Reedt Dortland AK, Giltay EJ, van Veen T, Zitman FG, Penninx BW. Metabolic syndrome abnormalities are associated with severity of anxiety and depression and with tricyclic antidepressant use. Acta psychiatrica Scandinavica. 2010;122(1):30-9.
33. Bekhbat M, Chu K, Le NA, Woolwine BJ, Haroon E, Miller AH, et al. Glucose and lipid-related biomarkers and the antidepressant response to infliximab in patients with treatment-resistant depression. Psychoneuroendocrinology. 2018;98:222-9.
34. Poongothai S, Pradeepa R, Ganesan A, Mohan V. Prevalence of depression in a large urban South Indian population--the Chennai Urban Rural Epidemiology Study (CURES-70). PloS one. 2009;4(9):e7185.
35. Agarwal A, Agarwal M, Garg K, Dalal PK, Trivedi JK, Srivastava JS. Metabolic syndrome and central obesity in depression: A cross-sectional study. Indian J Psychiatry. 2016;58(3):281-6.
36. Zigmond AS, Snaith RP. The hospital anxiety and depression scale. Acta psychiatrica Scandinavica. 1983;67(6):361-70.
37. Worboys M. The Hamilton Rating Scale for Depression: The making of a "gold standard" and the unmaking of a chronic illness, 1960-1980. Chronic illness. 2013;9(3):202-19
38. Hamilton M. Development of a rating scale for primary depressive illness. The British journal of social and clinical psychology. 1967;6(4):278-96.
39. Zimmerman M, Martinez JH, Young D, Chelminski I, Dalrymple K. Severity classification on the Hamilton Depression Rating Scale. Journal of affective disorders. 2013;150(2):384-8.
40. Nebhinani N, Sharma P, Suthar N, Pareek V, Kunwar D, Purohit P, et al. Correlates of metabolic syndrome in patients with depression: A study from north-western India. Diabetes & metabolic syndrome. 2020;14(6):1997-2002.
41. Grover S, Nebhinani N, Chakrabarti S, Avasthi A. Prevalence of metabolic syndrome among patients with depressive disorder admitted to a psychiatric inpatient unit: A comparison with healthy controls. Asian journal of psychiatry. 2017;27:139-44.
42. Hasin DS, Sarvet AL, Meyers JL, Saha TD, Ruan WJ, Stohl M, et al. Epidemiology of Adult DSM-5 Major Depressive Disorder and Its Specifiers in the United States. JAMA Psychiatry. 2018;75(4):336-46.