

# Study of Platelet Indices in Patients with Metabolic Syndromes: A Study Protocol

## Abstract:

**Background:** Metabolic syndrome is a syndrome of unified metabolic disorder which includes abdominal obesity (AO), hypertension, hypertriglyceridemia (HTG), hyperglycemia and decreased high-density lipoprotein (HDL). Metabolic syndrome subjects are exposed to greater chances to have insulin resistance, visceral fat accumulation, atherogenic changes to the vessels, abnormal lipid levels and abnormal functioning of endothelium. Platelets play a key role in hemostasis. The mean platelet volume (MPV) and platelet's proportion are indicators of platelet function. This study aims to find the correlation between various platelet indices in patients with Metabolic syndromes.

**Methods:** This prospective study is planned to be conducted in AVBRH, Wardha. Patients anthropometric parameters like height, weight, blood pressure, waist circumference, hip circumference and biochemical parameters such as fasting blood glucose, serum triglycerides, serum HDL, and mean platelet volumes will be assessed. Total 130 subjects will be assessed and data will be analyzed to estimate a correlation between platelet indices and metabolic syndromes.

**Expected Results:** A significant correlation is expected between various platelet indices in patients of different metabolic syndromes.

**Keywords:** Metabolic syndrome, Platelet indices, Obesity, Phenotypes, Anthropometric indicators, Correlation.

## Introduction:

Metabolic syndrome is a syndrome of unified metabolic disorder which includes abdominal obesity (AO), hypertension, hypertriglyceridemia (HTG), hyperglycemia and decreased high-density lipoprotein (HDL). WHO stated it first in year 1988<sup>1</sup>.

Multiple Studies conducted in India have shown that the risk factors for metabolic syndrome are prevalent thirty one point four percent for AO, forty five point six percent for HTG, sixty five point five percent w.r.t HDL, fifty five percent for elevated blood pressure, and twenty

six percent have raised fasting plasma glucose<sup>2</sup>. In study by Das M et al it was found that a prevalence of Metabolic Syndrome to be 31.4% and prevalence was higher in the females<sup>3</sup>

“The metabolic syndrome is defined on the basis of NCEP-ATP III criteria, this entails the following and needs 3 or more good outcomes to validate a diagnosis. Abdominal obesity: Waist circumference more than 80 cm inches for female and more than 90 cm for male Body mass index (BMI): exceeding 30 kg/m<sup>2</sup> and/or waist/hip ratio, greater than 0.09 for male and greater than 0.85 for female Elevated triglyceride levels: more than 150 mg/dL Decreased HDL levels: < 40 mg/dL for male and < 50 mg/dL for female , Elevated Blood Pressure levels: more than 130 mm Hg systolic or more than eighty five mm Hg diastolic, raised fasting glucose levels: 110-125, type 2 diabetes or impaired glucose tolerance or insulin resistance, denoted by hyperinsulinemia relative to glucose levels<sup>4</sup>.”

Metabolic syndrome subjects are exposed to greater chances to have insulin resistance, visceral fat accumulation, atherogenic changes to the vessels , abnormal lipid levels and abnormal functioning of endothelium . Insulin resistance patients usually cultivate HTG and are at higher risk of developing atheroma in lumen of vasculature, there may be increased incidence of coronary artery disease related events like stroke<sup>5</sup>.

The following are the causes of metabolic syndrome, were if present post as a highest risk factor

- Abdominal obesity (the waistline is large)
- A passive style of life
- Resistance to insulin

Some individuals are at risk of metabolic syndrome because they take medications that cause blood pressure, cholesterol levels and blood sugar levels to gain weight or alter. These medications are most commonly used in the treatment of asthma, allergies, Human immunodeficiency virus , anxiety, and other forms of mental illness [28].

Form of diabetes (Type 2) is a progressive condition arising from a complex relationship between inheritance and the environment and other risk factors, important risk factors being insulin resistance, obesity, cigarette smoking ,alcohol intake and body weight.

In patients with diabetes mellitus, altered platelets have been documented and MS has been regarded as A 'prothrombotic state' with increased reactivity of platelets. They have been linked to increased risk, Among such patients, vascular complications. Platelet indices are associated with platelet functional status. And a potential risk factor for diabetes and MS vascular complications

Metabolic Syndrome pathogenesis requires both hereditary and acquired variables that play a role in the final inflammatory pathway that leads to CVD. Owing to the dramatic rise in obesity worldwide, MetS has become increasingly important in recent times. In order to apply lifestyle and risk factor modification efficiently, early diagnosis is critical. The goal of Metabolic syndrome medication treatment is to treat the individual components of Metabolic syndrome, such as elevated blood pressure , atorvastatin and anti-diabetic drug (metformin). In the treatment of metabolic syndrome, certain natural compounds and dietary components, also called nutraceuticals, have been shown to have some utility.

Platelets have an imperative part in the maintenance of usual hemostasis; MPV & record of the platelets is recognized as indicators and factors of platelet function<sup>6</sup>. Procoagulant proteins like P-selectin and glycoprotein IIIa are expressed at Platelets surfaces<sup>7</sup>. Enormous platelets comprise impenetrable granules which behaves metabolically and enzymatically extra energetic as compared to minor ones having greater thrombotic potential. This may serve as junction amid increase in MPV and increase in thrombotic potential<sup>8</sup>. While several assessments of platelet activity has emerged but Many of these are time consuming and not cheap, for atherothrombosis, on the other hand ,It is easy to measure MPV, PDW and P-LCR on Automated routine hemograms are available at a low cost. The fast detection of patients with larger platelets is possible During normal and timely hematological examination and can be treated within the golden time.

In the maintenance of normal homeostasis, a very important role is played by the Platelets. This function is in turn indicated by the platelet indices. platelets which are Larger in size have a greater number of granules which are dense this in turn increases their potency and makes them thrombogenic. In platelets, there is no change in the amount or scale of granules over the lifespan of the platelet.. The increased value of MPV has been related to numerous diseases, such as metabolic syndrome, stroke(cerebrovascular accidents), coronary heart disease and diabetes mellitus (DM).. Few experiments have demonstrated that platelet indices in diabetics are considerably higher than in non-diabetic individuals. Using the blood cell counters, Platelet parameters have been measured in the laboratory. These include MPV, Platelet distribution width (PDW), Plateletcrit (PCT), and platelet-large cell ratio (P-LCR). The detection of prothrombotic stage of platelet can be done in early stages by using the newer hematological analyzers through these platelet parameters.<sup>9</sup>

#### **Rationale:**

It has been seen in multiple studies that the platelet indices are higher in patients with higher blood glucose values and also with dyslipidemia when compared with the normal healthy population. by studying the platelet indices in metabolic syndrome patient the present study

will help in determination of the association between platelet indices and components of metabolic syndrome.

Our study aims to evaluate platelet indices in patients with Metabolic syndrome, hence able to detect the complication much earlier, before the complications can fully evolve.

### **Objectives :**

- To study the correlation between platelet indices and various size & proportions of the human body.
- To study the correlation between platelet indices and independent variables including demographic factors (age, gender), Mets factors.

### **Methods:**

The cross sectional study will be conducted in Acharya Vinoba Bhave Hospital, Sawangi (Meghe) over a period of two years from 2020 to 2022.

### **INCLUSION CRITERIA:**

Patients satisfying criteria of Metabolic Syndrome according to NCEP-ATP III criteria and guidelines<sup>4</sup>." Patients giving consent for the same.

### **EXCLUSION CRITERIA:**

Patients not consenting, Patients who are already on anti-platelet treatment ,Patients refusing investigations ,Patients who are seriously ill.

### **Metabolic syndrome**

There have been several definitions of Metabolic syndrome, but the most commonly used criteria for definition at present are from NCEP-ATP III. The metabolic syndrome is defined on the basis of Diagnostic criteria by the " NCEP-ATP III- as mentioned in introduction<sup>4</sup>."

### **METHODS**

#### **ANTHROPOMETRIC MEASUREMENTS:-**

Anthropometric features including weight, height, BMI, waist circumference (WC),neck circumference(NC)

**WEIGHT**-Weight in kilograms will be recorded with a static patient on measuring scale without foot wear and with light clothing using portable weight scale and measuring inflexible bars with high accuracy.

#### **BLOOD PRESSURE:**

Blood pressure was recorded in the sitting position after 5 minutes of rest using standard mercury **manometer**.

**“High Blood Pressure is classified as readings of above 130 mm Hg for systolic blood pressure (SBP), or diastolic of above 80mmhg measurement, according to American Heart Association (AHA) guidelines.”. “Blood pressure of each patient was thus taken based on AHA-recommended protocol”.**<sup>10</sup>

#### **WAIST CIRCUMFERENCE:**

The circumference of the waist was measured at the midway between the lower border of the least palpable rib and the tip of the iliac crest using a non elastic tape that produced a constant 100-g tension. The tape was mounted around the body, but not so tightly pulled that it was constricting.. With arms on the sides, feet placed close together and weight uniformly spread around the feet, the patient was made to stand. The waist diameter was determined when the lungs are at their usable **residual potential at the end of a normal expiration. To minimise the tug of abdominal material** during the waist measurement, Before the actual calculation was completed, the patient was requested to relax and take a few deep, normal breaths.

#### **Neck circumference**

In the centre of the body, between the mid cervical spine and the mid anterior neck, the neck diameter will be determined to within 1 mm, with weekly calibration of plastic tape.<sup>11</sup> In men with a laryngeal prominence (Adam's apple), it will be measured only below the prominence. With the subjects standing erect, with the face guided forward and shoulders relaxed, all circumferences will be taken.<sup>12</sup>

#### **Collection of blood sample**

It was first disinfected by the skin over the median cubital vein, Applying surgical spirit, along with the cubital fossa, to the cubital fossa, Application of the proximal tourniquet to the fossa. Then the Blood was extracted with a sterile regular venipuncture needle. For sampling and full blood count in a potassium ethylene diamine tetra acetate bulb (EDTA), and was examined under fifteen minutes.

## Investigations:

### BIOCHEMICAL PARAMETER ESTIMATION

Platelet indices including plateletcrit, MPV, and PDW, BMI, waist circumference, Blood Pressure, Fasting lipid profile, Fasting Blood sugars, Post prandial Blood sugars

VARIABLE AND MEASUREMENT used are BMI:  $\text{weight}/(\text{height})^2$  expressed in  $\text{Kg}/\text{Mtr}^2$ , Weight, Blood pressure, Waist circumference.

### Sample size:

The sample size was calculated by the following formula

$$\text{Sample size } n = \frac{[\text{DEFF} * Np(1-p)]}{[(d^2/Z^2(1-\alpha/2)^2 * (N-1) + p*(1-p))]}$$

Where prevalence was 24.9% as per the study by Gupta R et al 19, the sample size was calculated to be 125 which will be rounded off to 130, with 99% confidence interval

Population size (for finite population correction factor or fpc) (N): 1000000 and Hypothesized % frequency of outcome factor in the population (p): 13.1% +/- 10

Confidence limits as % of 100 (absolute +/- %)(d): 10%

Design effect (for cluster surveys-DEFF): 1

### Expected Outcomes/Results:

This study aims at estimating correlation between platelet indices in patients of metabolic syndrome and results are expected to be equivalent to the studies done earlier. The previous studies have shown a significant increase in total leukocyte and neutrophil count and neutrophil/lymphocyte ratio (N/L) ratio in all groups of metabolic syndrome. A similar result is expected with platelet indices, where it showed significantly higher in all cases of metabolic syndrome.

### Discussion:

Metabolic syndrome (MS) is a syndrome of unified metabolic disorder which includes AO, hypertension, HTG, HG and decreased HDL.

Obesity is a noncommunicable disease and non-communicable diseases burden has been expanding in countries like India

In a study done in 2019 by Adel Abdel-Moneim<sup>10</sup> platelets count, PDW and MPV levels and platelets/lymphocyte ratio was ominously more among subjects with Metabolic Syndrome in comparison to the fit subjects. The research also indicated the essential role of platelet indices, leukocytes, as markers in the early detection of individuals with components of metabolic syndrome. Higher numbers of leukocytes and erythrocytes have raised the likelihood of metabolic syndrome in both sexes. Platelets were a safety factor for men, but platelets appeared to be a risk factor for women, as per study done by Pingping zhou et al<sup>13</sup>. The study aims at estimating correlation between platelet indices in patients of metabolic syndrome. Many studies related to various aspects of this study were reported<sup>15-20</sup>. Evidence of widespread problem of metabolic diseases is available from GBD studies<sup>21-27</sup>.

### **Conclusion :**

This examination will throw a light on whether Metabolic syndrome is a proinflammatory and prothrombotic state, portrayed by change of platelet indices. The study would help to suggest whether plateletcrit is demonstrated to be a factually critical biomarker alongside different boundaries, for example, midsection periphery, systolic pulse, and serum triglyceride levels. The study would help in establishing whether early detection and development of patients utilizing these markers can prompt a general decrease in morbidity and mortality inferable from MetS.

### **References:**

1. Alberti KG, Zimmet PZ. Definition diagnosis and classification of diabetes mellitus and its complications. Part 1: diagnosis and classification of diabetes mellitus provisional report of a WHO consultation. *Diabet Med* 1998;15:539–53.
2. Misra A, Khurana L. Obesity and the metabolic syndrome in developing countries. *J Clin Endocrinol Metab* 2008;93(11, Suppl 1):S9–S30
3. Das M, Pal S, Ghosh A. Association of metabolic syndrome with obesity measures, metabolic profiles, and intake of dietary fatty acids in people of Asian Indian origin. *J Cardiovasc Dis Res* 2010;1(3):130–135
4. Grundy SM, Cleeman JI, Daniels SR, et al; American Heart Association; National Heart, Lung, and Blood Institute. Diagnosis and management of the metabolic syndrome: an American Heart Association/National Heart, Lung, and Blood Institute scientific statement. *Circulation* 2005;112(17):2735–2752
5. Ford ES. The metabolic syndrome and mortality from cardiovascular disease and all-causes: findings from the National Health and Nutrition Examination Survey II Mortality Study.

6. Atherosclerosis 2004;173(2):309–314
7. Shimodaira M, Niwa T, Nakajima K, Kobayashi M, Hanyu N and Nakayama T. Correlation between mean platelet volume and fasting plasma glucose levels in prediabetic and normoglycemic individuals. *Cardiovasc Diabetol* 2013;12: 14.
8. Mathur A, Robinson MS, Cotton J, Martin JF, Erusalimsky JD. Platelet reactivity in acute coronary syndromes: evidence for differences in platelet behaviour between unstable angina and myocardial infarction. *Thromb Haemost.*2001;85:989-94.
9. Endler G, Klimesch A, Sunder-Plassmann H, Schillinger M, Exner M, Mannhalter C et al. Mean platelet volume is an independent risk factor for myocardial infarction but not for coronary artery disease. *Br J Haematol.* 2002;117:399-404.
10. Walinjar RS, Khadse S, Kumar S, Bawankule S, Acharya S. Platelet indices as a predictor of microvascular complications in type 2 diabetes. *Indian journal of endocrinology and metabolism.* 2019 Mar;23(2):206.
11. Abdel-Moneim A, Mahmoud B, Sultan EA, Mahmoud R. Relationship of leukocytes, platelet indices and adipocytokines in metabolic syndrome patients. *Diabetes & Metabolic Syndrome: Clinical Research & Reviews.* 2019 Jan 1;13(1):874-80.
12. Nardin M, Verdoia M, Barbieri L, De Luca G, Novara Atherosclerosis Study Group (NAS). Impact of metabolic syndrome on mean platelet volume and its relationship with coronary artery disease. *Platelets.* 2019 Jul 4;30(5):615-23.
13. Kumar, Sunil & Gupta, Apurva & Jain, Shraddha. (2012). Neck circumference as a predictor of obesity and overweight in rural central India. *International Journal of Medicine and Public health [Int. J. Med. Public health] | Vol 2| Issue 1 | 2012..* 1. 10.5530/ijmedph.2.1.11
14. Zhou P, Meng Z, Liu M, Ren X, Zhu M, He Q, Zhang Q, Liu L, Song K, Jia Q, Tan J. The associations between leukocyte, erythrocyte or platelet, and metabolic syndrome in different genders of Chinese. *Medicine.* 2016 Nov;95(44).
15. Chandak, S., A. Singh, and A. Belsare. "Study of Metabolic Syndrome in Patients of Acne Vulgaris." *International Journal of Pharmaceutical Research* 11, no. 1 (2019): 1223–28. <https://doi.org/10.31838/ijpr/2019.11.01.216>.
16. Gupta, A., R. Sarode, S. Kumar, and G.M. Dhopavkar. "Impact of Platelet Indices as Prognostic Markers of Sepsis." *International Journal of Pharmaceutical Research* 11, no. 3 (2019): 1413–17. <https://doi.org/10.31838/ijpr/2019.11.03.153>.
17. Gupte, Y., S. Acharya, S. Kumar, and P.S. Patil. "Assessment of Endothelial Function by Fmd (Flow Mediated Dilatation) in Prediabetes." *International Journal of Pharmaceutical Research* 11, no. 2 (2019): 1808–12. <https://doi.org/10.31838/ijpr/2019.11.02.202>.
18. Acharya, S., and S. Shukla. "Metabolic Healthy Obesity-a Paradoxical Fallacy?" *Journal of Clinical and Diagnostic Research* 12, no. 10 (2018): OE07-OE10. <https://doi.org/10.7860/JCDR/2018/36809.12165>.
19. Kirnake, V., A. Arora, P. Sharma, M. Goyal, R. Chawlani, J. Toshniwal, and A. Kumar. "Non-Invasive Aspartate Aminotransferase to Platelet Ratio Index Correlates Well with

- Invasive Hepatic Venous Pressure Gradient in Cirrhosis.” *Indian Journal of Gastroenterology* 37, no. 4 (2018): 335–41. <https://doi.org/10.1007/s12664-018-0879-0>.
20. Khatib MN, Kirubakaran R, Gaidhane S, Shankar AH, Quazi Syed Z. Yoga for improving functional capacity, quality of life and cardiovascular outcomes in people with heart failure. *Cochrane Database of Systematic Reviews* [Internet]. 2017;2017(7). <https://doi.org/10.1002/14651858.CD012015.pub2>.
  21. James, Spencer L, Chris D Castle, Zachary V Dingels, Jack T Fox, Erin B Hamilton, Zichen Liu, Nicholas L S Roberts, et al. “Estimating Global Injuries Morbidity and Mortality: Methods and Data Used in the Global Burden of Disease 2017 Study.” *Injury Prevention* 26, no. Supp 1 (October 2020): i125–53. <https://doi.org/10.1136/injuryprev-2019-043531>.
  22. James, Spencer L, Chris D Castle, Zachary V Dingels, Jack T Fox, Erin B Hamilton, Zichen Liu, Nicholas L S Roberts, et al. “Global Injury Morbidity and Mortality from 1990 to 2017: Results from the Global Burden of Disease Study 2017.” *Injury Prevention* 26, no. Supp 1 (October 2020): i96–114. <https://doi.org/10.1136/injuryprev-2019-043494>.
  23. Murray, Christopher J L, Cristiana Abbafati, Kaja M Abbas, Mohammad Abbasi, Mohsen Abbasi-Kangevari, Foad Abd-Allah, Mohammad Abdollahi, et al. “Five Insights from the Global Burden of Disease Study 2019.” *The Lancet* 396, no. 10258 (October 2020): 1135–59. [https://doi.org/10.1016/S0140-6736\(20\)31404-5](https://doi.org/10.1016/S0140-6736(20)31404-5).
  24. Murray, Christopher J L, Aleksandr Y Aravkin, Peng Zheng, Cristiana Abbafati, Kaja M Abbas, Mohsen Abbasi-Kangevari, Foad Abd-Allah, et al. “Global Burden of 87 Risk Factors in 204 Countries and Territories, 1990–2019: A Systematic Analysis for the Global Burden of Disease Study 2019.” *The Lancet* 396, no. 10258 (October 2020): 1223–49. [https://doi.org/10.1016/S0140-6736\(20\)30752-2](https://doi.org/10.1016/S0140-6736(20)30752-2).
  25. Vos, Theo, Stephen S Lim, Cristiana Abbafati, Kaja M Abbas, Mohammad Abbasi, Mitra Abbasifard, Mohsen Abbasi-Kangevari, et al. “Global Burden of 369 Diseases and Injuries in 204 Countries and Territories, 1990–2019: A Systematic Analysis for the Global Burden of Disease Study 2019.” *The Lancet* 396, no. 10258 (October 2020): 1204–22. [https://doi.org/10.1016/S0140-6736\(20\)30925-9](https://doi.org/10.1016/S0140-6736(20)30925-9).
  26. Gondivkar SM, Indurkar A, Degwekar S, Bhowate R. Evaluation of gustatory function in patients with diabetes mellitus type 2. *Oral Surgery, Oral Medicine, Oral Pathology, Oral Radiology, and Endodontology*. 2009 Dec 1;108(6):876-80.
  27. Khatib N, Gaidhane S, Gaidhane AM, Khatib M, Simkhada P, Gode D, Zahiruddin QS. Ghrelin: ghrelin as a regulatory Peptide in growth hormone secretion. *Journal of clinical and diagnostic research: JCDR*. 2014 Aug;8(8):MC13.
  28. Keerio, R. B., Abbas, S., Owais, M. A., Iqbal, M., Naqvi, S. S. Q. and Arain, A. G. (2021) “Frequency of Metabolic Syndrome and its Associated Factors in Patients with Breast Carcinoma at Tertiary Care University Hospitals of Pakistan”, *Journal of Pharmaceutical Research International*, 33(58A), pp. 527-533. doi: 10.9734/jpri/2021/v33i58A34148.