**Proposed Title of the Thesis**

**Occupational Exposure to Silica Dust and its Association with COPD**

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**Introduction**

The Global Initiative for Chronic Obstructive Lung Disease (GOLD) has defined Chronic obstructive pulmonary disease (COPD) is a common, preventable and treatable disease that is characterized by persistent respiratory symptoms and airflow limitation that is due to airway and/or alveolar abnormalities usually caused by significant exposure to noxious particles or gases.

chronic airflow limitation that is characteristic of COPD is caused by a mixture of small airways disease and parenchymal destruction the relative contributions of which vary from person to person(GOLD,2018). COPD includes emphysema and chronic bronchitis (john et al.,2011).

COPD is a global health concern and a major causes of chronic morbidity and mortality throughout the world. The Global Burden of Disease Study has projected that COPD, which ranked sixth as the cause of death in 1990, will become the third leading cause of death (Dhadke et al.,2015) and 5th common cause of morbidity all over the world by the year of 2020 (Helvaci et al.,2012).

The main risk factor for COPD is cigarette smoking .Other risk factors have also been implicated including exposure to industrial dust and fumes, outdoor air pollution (Blanc PD et al.,2009) second hand smoke & biomass smoke ( Blum A. et al.,2011) An estimated 15-30% of COPD cases are attributable to occupational exposures(Toren and Jarvholm, 2014).

Increased COPD risk has been associated with some specific occupational exposure agents, including : Silica (Tse et al., 2007; Dement et al., 2010), coal dust (Coggon and Newman Taylor, 1998), asbestos (Dement et al., 2010), Cement dust(Fell et al.,2010), diesel exhausts(Hart et al., 2009).

There is increasing evidence that lung function development is influenced both in utero and in the early years of life by factors such as maternal smoking, low birth weight, diet and nutrition (Boots A.W. et al.,2003).

Although tobacco smoking is the major risk factor for COPD with an estimated fraction of 80–90% (ATS, 1995a), only 15–20% of smokers develop COPD (Barr et al., 2002; Mannino et al., 2002). A significant fraction of all COPD cases and COPD-related mortality occurs among nonsmokers (Eisner et al., 2010).

According to the updates of the Global Initiative for Chronic Obstructive Lung Disease (GOLD),occupational exposure is one of the two most important risk factors for COPD (GOLD,2010). In developing countries such as India COPD due to non-smoking causes account to 30-50% of all COPD cases (Salvi & Barnes,2009).

Crystalline silica is found in stone, rock, sand, gravel and clay, as well as products such as bricks, tiles, concrete, artificial stone benchtops and some plastic materials .When these materials are worked on, the silica is released as a fine dust. This dust is respirable crystalline silica commonly called silica dust( Carey R.N. et al.,2014).

It has been found that crystalline silica is more dangerous because of its needle like structure which is cytotoxic and produce highly reactive surface radicals after grinding which favours the adsorption of surface materials. The severity of diseases depends upon the size, shape, concentration of particles and duration of exposure(Bushra Iftikhar et al.,2009).

The workers of stone quarry are exposed to silica dust of different concentration and particulate size. Average dust levels vary from about 0.5mg/m3 to over 10mg/m3. The studies suggest that loss of lung function occurs with exposures to silica dust at concentration of between 0.1 and 0.2mg/m3(Lesley R.,2007).

Inhalation of silica dust for long periods can causes focal and interstitial fibrosis, centrilobular emphysema and progressive massive fibrosis of lungs (Ralston et al., 2018).

It is also possible that workers exposed to silica have an increased risk of chronic bronchitis as a consequence of non-specific effects of dust (Seaton et al., 2000).

People with COPD suffering from chronic respiratory symptoms such as cough,sputum production and shortness of breath. They may also experience more systemic symptoms such as fatigue, weight loss, muscle weakness and anorexia. Depression and anxiety are also common and contribute to comorbidity (Stuart H,2018).Lung function decline, reduction in muscle strength, and reduced exercise capacity all contribute to increasing disability.

The most widely recommended diagnostic criteria for COPD used in clinical practice requires the presence of relevant symptoms and a compatible clinical history (history of smoking or other noxious exposures) together with objective measures of airflow obstruction as defined by a post-bronchodilator forced expiratory volume in one second (FEV1) to forced vital capacity (FVC) ratio of less than 0.7(Benfield T.et al.,2008)

A study was conducted in Peshaware, Pakistan on 160 workers of dust generating industries having exposure to silica dust for 5 years or more. The result showed, 56(35%) people were suffering from COPD among them 48 were smoker and 8 were non smoker(Bushra iftikhar et al.,2009).

Another study was conducted in Welsh, UK. In that study 1255 men participated among them 726 were slate miners expose to respirable crystaline silica and 529 were unexposed non miners. Result shows COPD was more common in miners(n=213,33%) than non miners(n=120,26%). After adjustment for smoking slate miners were associated with reduction of FEV1 and FVC and increase risk of COPD which is independent of smoking status(C.J.Reynolds et al., 2016).

Stone quarry is an important one among the industries that make the workers more prone to silica exposure. There are more than eight hundred stone quarries in Sylhet, mainly distributed in Bholaganj of Companiganj upazilla and Jaflong of Gowainghat upazilla which roughly employ more than one lac workers (Selim and Ali,2017).

But even with such large number of employees, stone quarrying remains an unorganized sector of industry.

Considering the fact that quarry industry has become one of the major employers of labour in Bholaganj and Jaflong, this study aims to determine the association of occupational exposure to silica dust with COPD among stone quarry workers of that area.

This study will also document the availability of health care facilities and safety measures at the site as ways of minimizing occupational health hazards associated with stone quarrying.

**Rationale**

Rapid industrialization, requiring heavy supplies of construction material like stones, bricks, cement producing silica dust in health endangering amounts. Cigarette smoking, lack of protective measures against silica dust inhalation and long hours of daily exposure are all adding significantly to the problem.

The workplace health hazard are an important public health issue and are avoidable through preventable intervention in the workplace. Although the developed nations have taken few steps forward to ensure safe and healthful working conditions by setting and enforcing standards, Bangladesh is still lagging behind.

Despite the fact that stone quarry industry has been the main way of earning livelihood for thousands of people in Sylhet, the occupation quite understandably posing some health risks too for the employees working there. Silica dust, being the most abundant particulate substance in the air of quarry areas, is likely to causing the chronic obstructive pulmonary diseases.

The purpose of this study is to ascertain the association between prolonged exposure to silica dust and COPD among the stone quarry workers of sylhet. The findings of this study will be beneficial in policy making and enforcing proper legislative measures, so that the health hazards of the quarry workers can be minimized in the future.

**Research Question**

Is silica dust responsible for COPD irrespective of smoking?

**Hypothesis**

* COPD can be caused by silica dust only irrespective of smoking.
* Silica dust act synergistically with smoking causing the chronic obstructive pulmonary diseases(COPD).

**Objectives**

**General Objective:**

To see the association between silica dust exposure and COPD among the stone quarry workers of sylhet.

**Specific Objectives:**

To establish the diagnosis of COPD by compitable history and spirometry.

To see the prevelance of COPD among the non smokers exposed to silica dust.

To see the prevelance of COPD among the smokers exposed to silica dust .

To assess the severity of COPD by GOLD severity scale 2008.

**Methodology**

**Study setting / place of study:**

The stone quarries of Companiganj and Gowainghat upazilla, Sylhet.

**Study period:**

one year after acceptance of the protocol.

**Study design:**

Cross sectional observational study

**Target population**: All stone quarry workers of sylhet.

**Study population**: Target population fulfilling the inclusion criteria within the study period.

**Sampling method:**

Convenient sampling.

Sample size is calculated using Cochran's formula considering 5% level of significance, 5% precision level (permissible error) and prevalence of chronic obstructive pulmonary diseases among stone quarry workers 13.7% (john dement et al., 2015).

The formula is: **n = Z2 pq / d2**

Where, n = estimated sample size

Z = 1.96 (in 95% Confidence Interval)

p = prevalence, 13.7% (0.137),

q = 1- 0.12 = 0.88,

d = permissible error, 5% (0.05)

(1.96)2 x 0.137 x 0.88

So,sample size (n) = -------------------------

(  0.05)2

= 184

Calculated sample size is 184 but in this study 200 samples will be taken.

**Inclusion criteria**

* Workers in the age range of 25 years to 60 years.
* Workers who have been working for at least five years in the quarry.

**Exclusion criteria**

* Workers with history of lung disease even before they started working at the quarry.
* Workers who are not interested to participate in the study.

**Variables**

* Main outcome variable:

association of silica dust with COPD.

* Confounding variables:

1. Duration of Smoking

2. Length of service

3. Use of biomass fuel in cooking

4. low birth weight

5. low soscioeconomic condition.

**Procedures of data collection**

* This study will be conducted on the stone quarries of sylhet, specifically on the quarries that have stone crusher machines.
* Total 10 visits will be made. On each visit, data will be collected from 20 respondents.
* Prior to each day of data collection an advocacy meeting will be arranged with the local elites and the respective industry owner. They’ll be informed in detail about the study and permission will be taken. An announcement will also be made on the day before data collection in the quarry area.
* After relevant history taking ,workers fulfilling the inclusion criteria will be informed about the study goals. Among them who’ll agree to participate voluntarily, will be taken as samples.
* Informed written consent will be taken from the respondents.
* Study population will be divided into two group: smoker and non smoker.
* Workers will be interviewed face to face using the semi-structured questionnaire.
* Baseline spirometry were performed for all the participants of the study. Spirometry will be carried out using a calibrated portable spirometer.
* Spirometry will be done with participants sitting at ambient temperature and after atleast 10 minutes of rest. The subjects will be asked to exhale into the spirometer as forcefully as possible after maximum inspiration.
* The parameters measured will be forced vital capacity (FVC) and forced expiratory volume in one second (FEV**1**). FEV**1**/FVC ratio will be calculated from the measured data.
* Study participants with value of FEV1/FVC of less than 0.7 were examined with post-bronchodilator test, which was performed according to the ATS / ERS guideline, 15 minutes after the administration of 400 micrograms of salbutamol.
* Subjects with forced expiratory volume in 1 second and forced vital capacity ratio (FEV1/FVC) value of less than 0.7 were regarded as COPD patients.
* The stages of COPD were also determined according to GOLD criteria.
* All relevant data will be recorded in data collection sheet designed for this study.

**Procedure of data analysis and interpretation**

* Data will be processed manually and analyzed with the help of SPSS (Statistical package for social sciences) Version 25.0
* Result will be tabulated and presented by appropriate method i.e. frequency table, bar chart and pie diagram etc.

**Quality assurance strategy**

All the data will be kept confidential. Only the researcher and ethical committee members will get full access to the data. Every records will be cross-checked by the supervisor.

**Ethical implications**

* The study protocol will be submitted for the approval of the ethical review committee of Sylhet MAG Osmani Medical College, Sylhet.
* Informed written consent will be taken from each of the respondents before taking any interview. A co-worker will be the witness of taking informed consent.
* The purpose and method of the study, confidentiality of the interviews, risks and benefits of participating in the study, respondent’s right to participate voluntarily and right to withdraw at any point will be explained in the local language from a printed handout.
* All information will be collected with complete respect to the worker’s wish and without any force or pressure.

**Result:** Result will be presented by appropriate tables graphs and charts.

**Discussion:** Discussion will be made comparing the result of the study with other study finding on relevant topics.

**Conclusion:** Conclusion will be drawn from result and discussion.

**Recommendation:** Recommendation will be made on the basis of findings.

**Flow Chart**

**Time table**

|  |  |  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
| **Activities** | **Month Year** | **Month Year** | **Month Year** | **Month Year** | **Month Year** | **Month Year** | **Month Year** | **Month Year** | **Month Year** | **Month Year** |
| **Designing the Study** | Sep, 2018 |  |  |  |  |  |  |  |  |  |
| **Review of Literature** | Sep, 2018 | Oct, 2018 | Nov, 2018 |  |  |  |  |  |  |  |
| **Development and Approval of Proposal** |  |  | Nov, 2018 |  |  |  |  |  |  |  |
| **Development of Data Collection Tools** |  |  |  | Dec, 2018 |  |  |  |  |  |  |
| **Pretesting Questionnaire** |  |  |  |  | Jan, 2019 |  |  |  |  |  |
| **Data Collection, Entry and Analysis** |  |  |  |  |  | Jan, 2019 to Dec, 2019 |  |  |  |  |
| **Report Writing** |  |  |  |  |  |  | Jan, 2020 |  |  |  |
| **Submission and Approval** |  |  |  |  |  |  |  | Feb, 2020 | March, 2020 |  |
| **Printing, Binding and Final Submission** |  |  |  |  |  |  |  |  |  | Apr, 2020 |

**Operational definitions**

* FEV**1**: the volume of air that the patient is able to exhale in the first second of forced expiration after a maximal inspiration
* FVC: the total volume of air that the patient can forcibly exhale in one breath after a maximal inspiration
* FEV**1**/FVC: the ratio of FEV**1** to FVC expressed as a percentage.
* COPD: Subjects with compatible history and forced expiratory volume in 1 second and forced vital capacity ratio (FEV1/FVC) value of less than 0.7 were regarded as COPD patients.

**Total budget**

* Spirometry: Tk. 1,50,000
* Travel to the site of data collection: Tk. 25,000
* Bronchodilator: TK.5,000
* Books and literature: Tk. 5,000
* Data analysis and compose: Tk. 10,000
* Printing and binding: Tk. 10,000

Total: Tk. 20,5000

References

* ATS. 1995a. Standards for the diagnosis and care of patients with chronic obstructive pulmonary disease.AmJ Respir Crit Care Med 152: S77–121.
* Benfield T, Lange P, Vestbo J. COPD stage and risk of hospitalization for infectious disease. Secondary COPD stage and risk of hospitalization for infectious disease 2008.
* Blanc PD, Menezes AMB, Plana E, et al. Occupational exposures and COPD: an ecological analysis of international data. Secondary Occupational exposures and COPD: an ecological analysis of international data 2009.
* Blum A, Simsolo C, Sirchan R, Haiek S. "Obesity paradox" in chronic obstructive pulmonary disease. Secondary "Obesity paradox" in chronic obstructive pulmonary disease 2011.
* Boots AW, Haenen GRMM, Bast A. Oxidant metabolism in chronic obstructive pulmonary disease. Secondary Oxidant metabolism in chronic obstructive pulmonary disease 2003. http://ovidsp.ovid.com/ovidweb.cgi?T=JS&PAGE=reference&D=med4&NEWS=N&AN=14621103.
* Barr RG, Herbstman J, Speizer FE, Camargo CA, Jr. 2002. Validation of self-reported chronic obstructive pulmonary disease in a cohort study of nurses. Am J Epidemiol 155:965–971.
* Bushra Iftikhar, Muhammad H., Hamid H.,Mahzar I.& Gulam sarwar.2009.`Relationship between silica dust exposure and COPD in workers of dust generating industries of distric peshware’ Gomal journal of medical science January-june 2009,vol.7 No.1,pp.46.
* Carey RN, Driscoll TR, Peters S, et al. Occup Environ Med 2014;71:55–62.
* Coggon D, Newman Taylor A. 1998. Coal mining and chronic obstructive pulmonary disease: A review of the evidence. Thorax 53:398–407.
* C. J. Reynolds, S. J. MacNeill, J. Williams, N. G. Hodges, M. J. Campbell, A. J. Newman Taylor and P. Cullinan, 2016, oxford university press on behalf of the society of occupational medicine.
* Dement JM, Welch L, Ringen K, Bingham E, Quinn P. 2010. Airways obstruction among older construction and trade workers at Department of Energy nuclear sites. Am J Ind Med 53:224–240.
* Dhadke VN, Dhadke SV, Raut N. Clinical Profile on Chronic Obstructive Pulmonary Disease Patients and Their Evaluation with Spirometry and 2D Echo. International Journal of Current Research 2015; 7(2): 12480-8
* Eisner MD, Anthonisen N, Coultas D, Kuenzli N, Perez-Padilla R, Postma D, Romieu I, Silverman EK, Balmes JR. 2010. An official American Thoracic Society public policy statement: Novel risk factors and the global burden of chronic obstructive pulmonary disease. Am J Respir Crit Care Med 182:693–718.
* Fell AK, Sikkeland LI, Svendsen MV, Kongerud J. 2010. Airway inflammation in cement production workers. Occup Environ Med 67:395–400.
* Global Initiative for Chronic Obstructive Lung Disease (GOLD). Global strategy for the diagnosis, management and prevention of COPD. Updated:on 2018. Global Initiative for Chronic Obstructive Lung Disease, Inc.
* Global Initiative for Chronic Obstructive Lung Disease. Global Strategy for the Diagnosis, Management, and Prevention of Chronic Obstructive Pulmonary Disease (Updated December 2010): Medical Communication Recourses, Ink. 2010. [displayed 22 November 2011]. Available at [http://www.goldcopd.com](http://www.goldcopd.com/)
* Hart JE, Laden F, Eisen EA, Smith TJ, Garshick E. 2009. Chronic obstructive pulmonary disease mortality in railroad workers. Occup Environ Med 66:221–226.
* Helvaci MR, Aydin LY, Aydin Y. Chronic obstructive pulmonary disease may be one of the terminal end points of metabolic syndrome. Pak J Med Sci 2012; 28: 376-9.
* John J. Reilly Jr, Edwin K Silverman, Stepen D Shapiro. 2011. Chronic Obstructive Pulmonary Disease. In: Longo D L., editor. Harrison’s principles of Internal Medicine. 18th edition. New York: Mc Graw Hill, p. 2142-6.
* Lesley Rushton. 2007`Chronic obstructive pulmonary diseases and occupational exposure to silica’,Reviews of envirnomental health,vol 22,No.4,pp.255-56,retrieved jan 2007.
* Mannino DM, Homa DM, Akinbami LJ, Ford ES, Redd SC. 2002. Chronic obstructive pulmonary disease surveillance-United States, 1971–2000. Respir Care 47:1184–1199.
* Ralston, S., Penman, I., Strachan, M. and Hobson, R. (2018). *Davidson's principles and practice of medicine*. 23rd ed. Churchill Livingstone Elsevier.
* Salvi SS, Barnes PJ. Chronic obstructive pulmonary disease in non-smokers. Lancet 2009;374:733-43.
* Seaton, A., Seaton, D., Leitch, A. and Crofton, J. (2000). *Crofton and Douglas's respiratory diseases*. 5th ed. Malden, Mass.: Wiley-Blackwell.
* Selim, M. and Ali, A. (2017). ’পাথর ব্যবসায় হরিলুট’, Jugantor, 26 February. [online] Available at: https://www.jugantor.com/news-archive/economics/2017/02/26/104354/%E0%A6%AA%E0%A6%BE%E0%A6%A5%E0%A6%B0-%E0%A6%AC%E0%A7%8D%E0%A6%AF%E0%A6%AC%E0%A6%B8%E0%A6%BE%E0%A7%9F-%E0%A6%B9%E0%A6%B0%E0%A6%BF%E0%A6%B2%E0%A7%81%E0%A6%9F [Accessed 29 Aug. 2018].
* Stuart, H., Penman, I., Strachan, M. and Hobson, R. (2018). *Davidson's principles and practice of medicine*. 23rd ed. Churchill Livingstone Elsevier.
* Toren K, Jarvholm B. 2014. Effect of occupational exposure to vapors, gases, dusts, and fumes on COPD mortality risk among Swedish construction workers: A longitudinal cohort study. Chest 145:992–997.

**Appendix-1**

**Data collection sheet**

SL.No : Date:

Name :

Age :

Sex : 1. Male 2. Female

Education :

Soscioeconomic cobdition:

Address : 1. Illiterate 2.Primary 3. Above

Mobile No :

**Thesis Protocol**

**Title:**

ASSOCIATION OF MEAN PLATELET VOLUME ( MPV) WITH DIABETIC RETINOPATHY (DR) IN TYPE 2 DIABETES MELLITUS (T2DM)

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**Introduction:**

Diabetes mellitus (DM) refers to a group of common metabolic disorders that share the phenotype of hyperglycemia. Depending upon the etiology of DM, factors contributing to hyperglycemia include reduced or absent insulin secretion, decreased glucose utilization, and increased glucose production. The metabolic dysregulation associated with DM causes secondary pathophysiologic changes in multiple organ systems that impose a tremendous burden on the individual with DM and on the health care system.**1** DM is a lifelong disease which increases morbidity, mortality and decreases quality of life.

According to International Diabetes Federation (IDF), in 2015, globally 415 million adults had diabetes. By 2040 this will rise to 642 million.**2** Estimates in 2015 indicate that global prevalence of DM is 8.8% and in South-East Asia it is 8.5% in the adult population.**2** Diabetes has become a major public health issue in Bangladesh, affecting one in ten adults.**3** National prevalence of DM in Bangladesh among 20-79 years aged is about 7.4%.**2** Prevalence of Diabetes in the rural population of Bangladesh is about 5.6%.**4**

Among the common types of DM ,Type 1 DM is characterized by absolute insulin deficiency affecting mostly the young individuals and Type 2 DM (T2DM) is characterized by resistance to the action of insulin and an inability to produce sufficient insulin to overcome this ‘insulin resistance’ due to progressive pancreatic β cell failure, which has higher incidence in adults.**1, 5**

Generally the chronic injurious effects of hyperglycemia are categorized broadly as macro vascular complications (coronary artery disease, peripheral arterial disease, and stroke) and micro vascular complications (diabetic retinopathy, diabetic nephropathy and diabetic neuropathy).**1, 6, 9**

Among the microvascular complications Diabetic Retinopathy (DR) is one of the highly specific & important complications with a worldwide prevalence of around 35% **7** and almost 18% prevalence in India**7** and about 21.6% in Bangladeshi rural population.**8** It is the most common cause of preventable blindness in adults in developed world. **9**

There is a clear relation of DR with duration of T2DM, poor glycemic status (HbA1c >7.0%) **24**  and hypertension.These three above mentioned conditions along with dyslipidemia, presence of diabetic nephropathy, obesity and smoking are the risk factors for DR **1, 9, 10, 24**

Clinically DR can be categorized in to non-proliferative (NPDR) and proliferative diabetic retinopathy (PDR) with or without maculopathy/macular oedema (MO).**1, 9**

NPDR is marked by vascular microaneurysms , dot & blot haemorrhages , cotton wool spots**1** & hard exudates.**9**

The known underlying pathologies for NPDR are loss of retinal pericytes, increased retinal vascular permeability, alterations or abnormal retinal blood flow, and abnormal retinal microvasculature ,all of which leads to retinal ischaemia, whereas, appearence of neovascularization in response to retinal hypoxia is the hallmark of PDR, where Vascular Endothelial Growth Factor (VEGF) play a key role. Various other growth factors like Platelet Derived Growth Factor (PDGF), concentration of which was found to be increased in vitreous of PDR patients, cause collagen synthesis and lead to neovascularization in PDR. These newly formed vasculature near the optic nerve and/or macula, easily rupture leading to vitreal haemorrhage and eventually lead to fibrosis and tractional retinal detachment that may cause sudden visual loss.**1, 9, 10**

Macular Oedema (MO) can occur at any stages of DR and is characterized by increased vascular permeability and deposition of hard exudates in the central retina. Clinically significant Macular Oedema (CSMO) is the most common cause of loss of vision in diabetic population.**1, 9,10**

DM has been recognized as a state of, “prothrombotic tendency” with increased platelet reactivity. **11, 15, 16, 21**

Platelets are tiny, disc-shaped, non-nucleated, flattened structures, 1-5 μm**12** in diameter. They are derived from cytoplasm of megakaryocytes. Primary function of platelet is formation of platelet plug in vascular injury.

Generally, the normal platelet count varies between 150,000 and 400,000/μl and normal platelet size varies between 7.5 and 10.5 fl.**13** The size of the platelets depends largely on the density of the granules present in them.**13,21** Mean platelet volume (MPV) is a platelet index which reflects the average size of platelets in a blood sample which can be quantified by clinical hematology analyzers from a complete blood count. **14**

According to several recent studies , hyperglycemia or uncontrolled DM causes larger platelets.**11, 16-22** The larger platelets has been reported to be secondary to the increased ploidy (DNA content) of Megakaryocytes.**15,16** Larger platelets are more active and aggregable than normal platelet and release more prothrombotic factors such as thromboxane A2 which play a key role in development of vascular complications in DM that correlates with the rise of MPV and supports the relevance of the MPV as a measure of platelet function or activity. **11, 14, 16-22, 25-29** In two recent Bangladeshi studies, Pervin et. al.**30** reported an association of increased MPV with Acute Coronary Syndrome (ACS) and Karim et al. **31** showed a positive association of Platelet Distribution Width (PDW) (which is another platelet index and also a marker of platelet activation) with Type2 DM only in male diabetic patients. But, published data about association of MPV with any microvascular complications like Diabetic Retinopathy in Type 2 DM are very limited worldwide and also not available in our settings.

**RATIONALE**

MPV is a simple, almost effortless, and relatively cheap method which can be easily studied with an hematology autoanalyzer .

Literature survey reveals there is clear association of MPV with uncontrolled T2DM and macrovascular complications.**11, 14, 16-21, 23** But, there are only few published data which establishes association of MPV with microvascular complications of diabetes specially with Diabetic Retinopathy. **32-39** Some of these literatures **32,36,39** recommended that MPV can be used as a low cost investigation to predict initially asymptomatic diabetic microvascular complicationslike diabetic retinopathy, risk of which increases with higher MPV values.

Therefore, this study is designed to explore the scientific knowledge about association of Mean Platelet Volume (MPV) with Diabetic Retinopathy in Type2 Diabetes Mellitus patients in our context.

**REASEARCH QUESTION**

Is there any association of Mean Platelet Volume (MPV) with Diabetic Retinopathy (DR) in Type 2 Diabetes Mellitus (T2DM) ?

**REASERCH OBJECTIVES**

A. General objectives:

* To evaluate Mean Platelet Volume (MPV) in Type 2 Diabetes Mellitus with or without Diabetic Retinopathy.

B. Specific objectives:

* To findout MPV level in diabetic group (already diagnosed or new cases**24**)
* To determine the MPV level in healthy non diabetics in our settings.
* To findout ‘controlled’**24** and ‘uncontrolled’**24** type 2 diabetic patients.
* To compare MPV level in controlled and uncontrolled T2DM.
* To see the duration of Diabetes.
* To see variation of MPV level with duration of Diabetes.
* To findout Diabetic Retinopathy (DR).
* To see association of MPV level with Diabetic Retinopathy (DR) in type 2 DM**.**

**METHODOLOGY**

* **Study Design:**

Cross Sectional observational study

* **Place of the study:**

Department of Medicine, Endocrinology outpatient department (OPD) & Ophthalmology OPD , Sylhet MAG Osmani Medical College Hospital, Sylhet.

* **Study Period:**

From June 2017 to May 2018

* **Target Population:**

Type 2 Diabetic patient attending Inpatient and Outpatient department of Medicine &

Endocrine & Ophthalmology outpatient department.

* **Study Population:**

Target population fulfilling the inclusion criteria within the given period will be

considered as study population.

* **Sample size:**

Sample size is calculated using Cochran's formula considering 5% level of significance, 5% precision level (marginal error) and considering prevalence of Type 2 DM in Bangladesh as 7.4% **2**

The formula is

 Where,

n = estimated sample size

z = 1.96 (in 95% Confidence Interval)

p = prevalence of T2 DM in Bangladesh =7.4% (0.074)

q =1-p= 1- 0.074= 0.926

d = admissible error (marginal error) considered as 5 % (0.05)

Therefore, the estimated sample size is

(1.96)2 X 0.074X 0.926

= 105.29

(0.05)2

So, Calculated sample size is 105.

* **Sampling Method :**

Convenience sampling method

* **Inclusion Criteria:**

All patients above 35 years of age having Type2 DM (old & new) with or without Diabetic Retinopathy.

* **Exclusion Criteria:**
* Other types of DM & Diabetic patients under 35 years
* Patient admitted with macrovascular complications of T2DM.
* Reduced platelet number (<150×103/µL) or any platelet disorder
* Anemia (<13mg/dl in male & <11.5 mg/dl in female) or anemia from any suspected/known bone marrow disorder or known hemoglobinopathies.
* Chronic systemic inflammatory conditions or high CRP
* Known case of any infectious disease/ sepsis
* Admited with acute disorders related to severe hyperglycemia [diagnosed cases of Diabetic Ketoacidosis (DKA) or Hyperglycemic Hyperosmolar State (HHS)]
* Known cases of Chronic Kidney Disease(CKD)/End stage renal disease(ESRD)
* Known Cirrhosis or Clinical stigmata of Chronic Liver Disease on examination
* Known or suspected thyroid- related disorders
* Known cases of AIDS
* Pregnant women
* Patients on anti-platelet drugs
* On/recent cancer chemotherapy
* Recent major surgery
* Other causes of vision loss e.g. congenital, mature cataract and glaucoma,etc.
* Refusal to take part in this study.

**Data Collection:** Data will be collected in a pre-designed data collection sheet.

**Preparation of questionnaire:** Standard questionnaire will be designed with a view to collect patient's medical records (Appendix-I).

**Procedure of Data collection:**

Before assessment informed written consent will be obtained from the patients after full explanation of the disease condition, methods of available treatment and their outcomes and purpose, procedure, benefit and risk of the study.

Detailed clinical history with special emphasis on symptoms related to microvascular complications of DM specially Diabetic retinopathy will be asked, proper clinical examinations & investigations will be done when a known or suspected case of type-2 DM , above 35 years of age will be found .

The newly diagnosed cases of type-2 DM will be made from history, clinical examination and biochemical parameters according to American Diabetic Association (ADA) criteria for diagnosing DM **24**. Chances of being type 1 DM , gestational diabetes and other specific type diabetes mellitus will be ruled out through history, examination and previous medical records.

For determining MPV in healthy non diabetic population in our settings, 20 of age and sex matched non-diabetic apparently healthy population such as doctors, nurse, other staffs of the Department of Medicine will be selected as control who are having FPG < 5.6 mmol/L (<100 mg/dL) and with no known visual problem to determine MPV level in our settings.

The total sample (n=105), will be divided into two groups namely HbA1c≤7 (Controlled) **24** [Group-A] and HbA1c>7 (Uncontrolled) **24** [Group-B] and again into T2DM without DR [Group-C] & T2DM with retinopathy [Group-D] and MPV levels will be studied in all groups & will be compared in between Group A & B and Group C & D, where already determined MPV level in healthy no diabetic adults will serve as baseline value.

Diabetic Retinopathy (DR) will be detected by dilated fundoscopy, which will be done by researcher himself with “Keeler Professional Ophthalmoscope” (made in UK) ,where pupil dilatation will be done by Tropicamide1%,1 drop in each eye, 20-30 minutes prior to examination. Findings will be verified by a qualified ophthalmologist (Resident Surgeon, Outpatient Department of Ophthalmology, SOMCH) and fundal photograph will be taken where applicable which will be done in a single private laboratory by researcher’s own cost to confirm the findings.

MPV levels variation will also be observed in respect of duration of diabetes, presence of hypertension, dyslipidemia , smoking status and demographic variables.

**Laboratory Procedure :**

The patients will be asked to take normal diet with no carbohydrate restriction for consecutive 3 days and then to come in the morning after overnight fasting (at least 8 hrs). Venous blood samples (2-3 ml) will be withdrawn under aseptic precaution in the fasting state to measure plasma glucose levels & fasting lipid profile. Samples for Complete Blood Count (CBC) [to see mean platelet volume (MPV)], HbA1c, Serum creatinine will be withdrawn at the same time by researcher himself and after breakfast at 2 hours (120 minutes) of breakfast another blood sample (3 ml) will be collected for 2-h After Breakfast Plasma Glucose ( 2-h ABF).

For 2-h PG after 75-g OGTT sample immediately after FPG, 75 gram glucose will be given orally in 250 ml of water and blood sample (2 ml) will be collected at 120 minutes according to WHO protocol.**5**

FPG/ 2-h PG will be done by using enzymatic hexokinase oxidation reference method for plasma glucose levels. Sample for fasting plasma glucose/2-h PPG estimation and Complete Blood Count (to see MPV) will be collected in sodium fluoride and tri-potassium salt of EDTA respectively.

Estimation of HbA1C will be done using auto analyzer (SD A1c Care, SD Biosensor, Korea) in College Pathology Lab which is based on immunoassay for hemolyzed whole blood & it is NGSP(National Glycohemoglobin Standardization Programme) & IFCC(International federation of Clinical chemistry) certified ,and reports will be given in DCCT (Diabetes Control and Complication trial) prescribed unit.

MPV will be estimated by collecting 3ml venous blood samples for complete blood count (CBC) using automated blood cell count analyzers (Sysmex XS 500i, Japan) in our College Pathology Lab, which uses Fluorescence flow cytometry for high quality analysis.

Glucose estimation, Serum Creatinine & Fasting Lipid Profile will be carried out by Automated Biochemistry Analyzer (Vitros 350, Orthoclinical Diagnostics,USA) in the same Lab. Tests will be conducted within 2 hours of sample collection from all the subjects.

All these investigations will be carried out in SOMC college pathology laboratory during office hours with prior permission of concerned authorities & kind cooperation of Department of Pathology, SOMC. Urine routine examination will be done in hospital pathology lab. ECG will be carried out by 12 channel ECG machine available in hospital and will be interpreted by researcher himself. All investigations will be done free of cost on academic interest or from researcher’s own budget.

CRP (C-Reactive Protein) and ACR (Albumin Creatinine ratio) (as not available in any labs of SOMC/SOMCH) will be carried out in a single, reputed private laboratory by researcher’s own cost in all cases. Spot ACR will be done if initial bed side heat coagulation test is found negative.

**Data Recording:**

Relevant data from history, physical examination and investigations will be recorded in predesigned case record form which will be filled up by the investigator himself.

**Variables:**

* **Study variables**
  + Mean Platelet Volume (MPV)
  + Diabetic Retinopathy
  + HbA1c (Glycated Hemoglobin)
  + Duartion of Diabetes
  + Fasting plasma glucose (FPG)
  + 2-Hours (After Breakfast) Plasma Glucose (2-h PG)
  + Hypertension (HTN)
  + Dyslipidemia
  + Smoking stutus
  + ACR (Albumin Creatinine ratio)
  + Clinical findings of diabetic neuropathy
* **Demographic variables:**
  + - Age
    - Sex
    - BMI (kg/m2)

**Quality Assurance**

Regular instruction from the supervisor will be taken. Collected data will be checked periodically.

**Quality control in laboratory**

Will be done by verifying reproducibility of the method through analyzing identical samples. Regular random comparing with other laboratories will also be done.

**Flow Chart:**

**Flow chart for the Steps of study**

Target population

Inclusion and exclusion criteria

Study population

Baseline MPV in Healthy controls, n=20

T2DM, n=105

History, Clinical Examination, Investigations

MPV in T2DM

Uncontrolled T2DM (Group-B)

Controlled T2DM ( Group-A)

MPV level

Without DR (Group-D)

With DR (Group-C)

Data collection

MPV level

Data collection

Data analysis

Result

**Data analysis and interpretation**

* Data will be processed and analyzed manullay and with the help of SPSS(Statistical Package for Social Science) version 22.0
* Quantitative data will be expressed as mean and standard deviation.
* Qualitative data will be expressed as frequency and percentage.
* Appropriate test & analysis will be done to find out level of significance and correlation.
* A probability ‘p’ value of < 0.05 will be considered as significant.

**Ethical Implication:**

* Ethical clearance will be taken from the ethical committee of Sylhet MAG Osmani Medical College prior to commencement of study.
* Informed written consent will be taken from the patients and study related information will be explained in local language to patients.
* Before data collection, the respondents will be told that they are at liberty to participate and to decline to answer any question during the study. The respondents will be given assurance that the findings of the interview/ investigation/ examination will not be used/ disclosed to any unauthorized person or authority other than the research purpose.

**Result:** Result will be presented by appropriate tables and figures.

**Discussion:**  Discussion will be made comparing the result of the study with other study finding on relevant topics.

**Conclusion:** Conclusion will be drawn from result and discussion.

**Recommendation:** Recommendation will be made on finding of the study**.**

**Operational Definitions:**

**Diabetes Mellitus:** In this study, diagnosis of T2 DM will be established by “2017 ADA criteria for diagnosing DM” **22**

**American Diabetes Association(ADA) criteria for diagnosing Diabetes:**

**1)** FPG(Fasting Plasma Glucose) ≥126 mg/dL (7.0 mmol/L). Fasting is defined as no caloric intake for at least 8 h.\*

OR,

**2)** 2-h PG≥200 mg/dL (11.1 mmol/L) during an OGTT. The test should be performed as described by the WHO, using a glucose load containing the equivalent of 75 g anhydrous glucose

dissolved in water.\*

OR,

**3)** A1C≥6.5% (48 mmol/mol). The test should be performed in a laboratory using a method that

is NGSP certified and standardized to the DCCT assay.

OR,

**4)** In a patient with classic symptoms of hyperglycemia or hyperglycemic crisis, a random plasma glucose ≥200 mg/dL (11.1 mmol/L).

\*In the absence of unequivocal hyperglycemia, results should be confirmed by repeat testing.

**Controlled Daibetes:** here, controlled diabetes is defined asdiabetic patients having HbA1c ≤7.0%.**22**

**Uncontrolled Diabetes:** Here, Uncontrolled diabetes is defined as HbA1c >7.0% .

**Diabetic Retinopathy:** Patients having at least two microaneurysms (arises from venous end of capillaries & appear as discrete, circular, dark red dots near to, but apparently separate from, the retinal vessels and no wider than a vessel at the optic disc margin ) and/or retinal hemorrhage(blot haemorrhage) (Larger than a microaneurysm, with indistinct margins and at least as wide as a vessel at the optic disc margin, these occur in deeper layers of the retina) /cotton wool spot(capillary infarcts of the nerve-fiber layer)/ hard exudates (leakage of lipoproteins )/intraretinal microvascular abnormalities /venous beading (saccular dilatation of venules )/new retinal vessels/pre-retinal or vitreous hemorrhages and/or macular exudates/oedema will be accepted as DR on iniatial fundoscopy and will be divided to NPDR & PDR with/without Maculopathy.**9** Futher confirmation & staging will be done with the help of qualified Ophthalmologist with repeat fundoscopy & fundal photograph.

**CSMO:** Clinically significant macular oedema is defines as hard exudates/thickening is 1 disc area or larger and if within 1 disc diameter of centre .

**Diabetic Nephropathy:** will be suspected if early morning spot ACR is > 30µg/mg creatinine in a spot sample of urine

**Diabetic Neuropathy:** will be considred ifany polyneuropathy (motor/sensory), mononeuropathy and/or autonomic neuropathy related to uncontrolled T2DM is found.

**Hypertension:** known hypertensive or patients having 2 readings of office blood pressure ≥140/90 mm of Hg.

**Dyslipidemia:** LDL (Low Density Lipoprotein): >100mg/dL, HDL(High Density Lipoprotein) <40mg/dL in male & <50 mg/dL in female, TG(Triglyceride) >150 mg/dL

**BMI:** Body mass index will be calculatedby equation =Weight in Kilogram / Height in meter2. According to World Health Organization (WHO) recommendation for Asians, BMI>23.0 kg/m2 will be considered as overweight and >25.0 kg/m2 will be considered as obese.

**References:**

* + 1. Kasper DL , Fauci AS, Hauser SL, Longo DL, Jameson JL,Loscalzo JL et al.; Harrisons principles of internal medicine, diabetes mellitus. 19th ed. USA,McGraw-Hill 2015 ; 417: 2399
    2. International Diabetic Federation, IDF Diabetes Atlas,7th ed. 2015:50-126 <http://www.diabetesatlas.org/>
    3. AkterS, Md. Rahman M,  Abe SK , SultanaP. Prevalence of Diabetes and Prediabetes and their risk factors among Bangladeshi Adults: a nationwide Survey.Bull World Health Organ 2014,92:204-213A
    4. Rahim MA, Rahaman ML, Mostafa AW,Ahmed SF. The Prevalence Rate of Diabetes Mellitus(DM) in Rural Population of Bangladesh. Dinajpur Medical College Journal2011,4:41-8
    5. 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(7):539- 53.
    6. Baynest HW. Classification, Pathophysiology, Diagnosis and Management of Diabetes Mellitus. J Diabetes Metab 2015;6(5).
    7. Yau JWY, Rogers SL, Kawasaki R,et al. Global Prevalence and Major Risk Factors of Diabetic Retinopathy. 2012;35.
    8. Akhter A, Fatema K, Ahmed SF, Afroz A, Ali L, Hussain A. Prevalence and associated risk indicators of retinopathy in a rural Bangladeshi population with and without diabetes. Ophthalmic Epidemiol. 2013;20(4):220–7.
    9. Stanley D. Davidson ’ s, Davidson’s Principle &Practice of Medicine,22nd edition, 2014 : 818-854.
    10. Aiello AM, Ocular complications of Diabetes Mellitus. In: Kahn CR, Weir GC, King GL, Jacobson AM, Moses AC, Smith RJ.et al; Joslin’s Diabetes Mellitus ,14th edition :905-919
    11. Zuberi BF, Akhtar N, Afsar S; Comparison of mean platelet volume in patients with diabetes mellitus, impaired fasting glucose and nondiabetic subjects. Singapore Med J. 2008; 49 (2): 114.
    12. Konkle BA, Disorder of platelet and vessel wall, In: Harrisons principles of internal medicine, 19th ed. USA, McGraw-Hill 2015 ; 725,741
    13. Calverley DC, Thienelt CD. Platelet structure and function in Haemostasis and thrombosis. Wintrobe's Clinical Haematology. 12th ed. Philadelphia: Lippincott Williams & wilkins; 2009;490-527**.**
    14. Hekimsoy Z, Payzin B, Ornek T and Kandogan G. Mean platelet volume in Type 2 diabetic pa­tients. J Diabetes Complications 2004; 18: 173-176.
    15. Brwon SA, Hong Y, Belder Ad, et al. Megakaryocyte ploidy and platelet changes in human diabetes and atherosclerosis.Arteriosclerosis, Thrombosis and Vascular Biology; 1997;17(4):802-807
    16. Defronjo RA ,Ferrannini E, Keen H, Zimmet P, et al.International Textbook of Diabetes Mellitus.3rd ed.2004; 2:1429
    17. Dubey I, Gaur BS, Singh R. A study to find correlation of platelet indices with HbA1c in diabetic patients with absence/presence of vascular complications. Int J Res Med Sci.2017;5(3):1042–7.
    18. Radha RKN, Selvam D. MPV in Uncontrolled & Controlled Diabetics- Its Role as an Indicator of Vascular Complication. Journal of clinical & Diagnostic Research 2016;10(8):22–6.
    19. Ulutas KT, Dokuyucu R, Sefil F, Yengil E, Sumbul AT, Rizaoglu H. Evaluation of mean platelet volume in patients with type 2 diabetes mellitus and blood glucose regulation : a marker for atherosclerosis? Int J Clin Exp Med.2014;i(4):955–61.
    20. Koddiatte TA, Manlkyam UK, Rao SB, et al. Mean Platelet Volume in Type 2 Diabetes Mellitus. J Lab Physicians.2012;i(1):5-9.
    21. Buch A, Kaur S, Nair R, Jain A. Platelet volume indices as predictive biomarkers for diabetic complications in Type 2 diabetic patients. J Lab Physicians. 2017;9(2):84.
    22. Ferroni P, Basili S, Falco a, Davì G. Platelet activation in type 2 diabetes mellitus. J Thromb Haemost. 2004;2(8):1282–91.
    23. Hasan Z, Hegde S, Uday I, Jayakumar NM, Anantharajaiah PH. Assessment of Mean Platelet Volume in Type 2 Diabetes Mellitus and Prediabetes. 2016;i(3):3–6.
    24. American Diabetes Association. Standards of Medical Care in Diabetes 2017. 2017;40(suppl. 1):S13,S50,S91-92
    25. Thompson CB, Eaton KA, Princiotta SM, Rushin CA, Valeri CR. Size dependent platelet subpopulations: relationship of platelet volume to ultrastructure, enzymatic activity and function. Br J Haematol.1982;50:509-19.
    26. Colwell JA and Nesto RW. The platelet in diabe­tes: focus on prevention of ischemic events. Diabetes Care 2003; 26: 2181-2188.
    27. Vinik AI, Erbas T, Park TS, Nolan R and Pit­tenger GL. Platelet dysfunction in type 2 diabe­tes. Diabetes Care 2001; 24: 1476-1485.
    28. Davi G, Santilli F, Vazzanna N. Platelets.3rd ed.London:Elsevier; 2013.Diabetes mellitus:711–31.
    29. Bhanukumar M, Ramaswamy PKH,Peddi NK, MenonVB. Mean Platelet Volume and Platelet Distribution Width as Markers of Vascular Thrombosis in Type 2 Diabetes Mellitus. 2016;50(September):127–31.
    30. Pervin S, Ferdousy S, Hossain M, Ai J, Sultana T. Elevated mean platelet volume is a marker of acute coronary syndrome. 2013;i(2):45–50.
    31. Karim F, Qs A, Jahan S, Khanam A, Rahman F. Estimation of platelet distribution width in type 2 diabetic male subjects. 2016;45(3):3–6.
    32. Citirik M, Beyazyildiz E, Simsek M. MPV may reflect subcinical platelet activation in diabetic patients with and without diabetic retinopathy. 2014;29(3):376–9.
    33. Ayhan Tuzcu E, Arıca S, Ilhan N, Daglioglu M, Coskun M, Ilhan O, et al. Relationship between mean platelet volume and retinopathy in patients with type 2 diabetes mellitus. Graefe’s Arch Clin Exp Ophthalmol;252(2):237–40.
    34. Dobbie JG, Kwaan HC, Colwell J, Suwanwela N. Role of Platelets in Pathogenesis of Diabetic Retinopathy. Arch Ophthalmol .1974 ,91(2):107–9.
    35. Güngör AA, Gürsoy G, Güngör F, Bayram SM, Atalay E. The relationship of mean platelet volume with retinopathy in type 2 diabetes mellitus. 2016; 1292–9.
    36. Yilmaz T, Yilmaz A. Relationship between Altered Platelet Morphological Parameters and Retinopathy in Patients with Type 2 Diabetes Mellitus. 2016;2016(Mi).
    37. Dindar S, Cinemre H, Sengul E, Annakkaya AN. Mean Platelet Volume is Associated with Glycaemic Control and Retinopathy in Patients with Type 2 Diabetes Mellitus 2013;i(6).
    38. Ateş O, Kiki İ, Bilen H, Keleş M, Koçer İ, Kulaçoğlu DN, et al. Association of Mean Platelet Volume With The Degree of Retinopathy in Patients with Diabetes Mellitus. Eur J Gen Med. 2009;6(2):99–102.
    39. Bae S H,Lee J,Roh K H, Kim J. Platelet Activation in Patients with Diabetic Retinopathy. Korean J ophthalmol.2003.17:140-14
    40. Demirin H, Ozhan H, Ucgun T, Celer A, Bulur S, et al. Normal range of mean platelet volume in healthy subjects:Insight from a large epidemiologic study. Thrombosis research ,2011;128(4):358-60

**TIME SCHEDULES :**

|  |  |  |  |  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
| **Activities** | **Sept**  **2016** | **Oct**  **2016** | **Nov**  **2016** | **Dec**  **2016** | **Jan2017**  **to**  **May2017** | **June2017**  **to**  **May 2018** | | | **J**  **U**  **N**  **E**  **2**  **0**  **1**  **8** | **JULY 2018** | **A**  **U**  **G**  **U**  **S**  **T**  **2018** | |
| Problem definition |  |  |  |  |  |  |  |  |  |  | |  | |
| Approach to problem |  |  |  |  |  |  |  |  |  |  | |  | |
| Research design |  |  |  |  |  |  |  |  |  |  | |  | |
| Questionnire testing |  |  |  |  |  |  |  |  |  |  | |  | |
| Lab investigations |  |  |  |  |  |  |  |  |  |  | |  | |
| Data collection |  |  |  |  |  |  |  |  |  |  | |  | |
| Data analysis |  |  |  |  |  |  |  |  |  |  | |  | |
| Report writing & binding |  |  |  |  |  |  |  |  |  |  | |  | |
| Submission |  |  |  |  |  |  |  |  |  |  | |  | |

**BUDGETING:**

|  |  |
| --- | --- |
| Cost of investigations & Instrument purchase | Tk. 150,000.00 |
| Internet search | Tk. 5,000.00 |
| Books and literature | Tk. 5,000.00 |
| Travelling | Tk. 5,000.00 |
| Data analysis and compose | Tk. 15,000.00 |
| Printing and binding | Tk. 10,000.00 |
| **Total** | **Tk 190,000.00** |

**Appendix- I**

**Data Collection Sheet:**

**Sl. No: Reg No: Date:**

**OPD/ IPD : Ward no : Unit :**

**Bed no : Hosp. Reg. no :**

**Name:**

**Address:**

**Age:** ………years.

**Sex:** 1. Male 2. Female

**Marital status:** 1.Married 2.Unmarried 3.Widow 4.Separated 5.Divorced

**Education:**

**Occupation:** 1. Service 2. Business 3.Farmer 4. Student,5. House wife 6. Daylabourer

7. Unemployed 8. Others.

**Economic Background:** Average income:

**Social background:**  1. Rural 2. Urban

**Smoker :**  1.Yes 2.No (…….pack/year)

**Anthropometric Measurement:**

1. Height (cm): ………………… cm
2. Weight (kg): ……………….kg
3. BMI (kg/m²):………………

**Pregnant:** Yes / No

**Duartion of Daibetes:** (new/months/years):

**Comorbidities:**

Hypertension : Yes / No

Cardiac disease : Yes / No

Chronic illness : Yes / No

Kidney disease : Yes / No

Liver disease : Yes / No

Thyroid disorder : Yes / No

Foot Ulcer : Yes / No

**Clinical Examination:**

1. Anaemia: Yes/No
2. Jaundice: Yes/No
3. Cyanosis: Yes/No
4. Oedema: Yes/No
5. Dehydration: Yes/No
6. Clubbing:
7. Koilonychia:
8. Leukonychia:
9. Lymphnodes:
10. Thyroid gland:
11. Pulse (beats/minute) (including peripheral pulses):
12. Blood Pressure (mm of Hg): Sitting:….../………Standing:…../…… Postural Drop:……..
13. Skin condition:
14. Foot ulcer:
15. Deformity:
16. Acanthosis nigricans:…..

If present, site:………

1. Bed side Heat coagulation test:………

18. Fundoscopy findings:

a) microaneurysms ……..Yes/No

b) dot & blot haemorrhages …...Yes/No

c) cotton wool spots……..Yes/No

d) hard exudates……..Yes/No

e) venous beading  ……..Yes/No

f) neovascularization  ……..Yes/No

g) macular Oedema/Exudate(CSMO) ...…Yes/ No ,

h) viteous haemmorahge…....Yes/No

19. Other neurological findings::

Muscle bulk: Normal/reduced Muscle tone:

Muscle Power: Reflexes:

Touch sensation: Normal/Impaired Vibration sense: Normal/Impaired

Joint position sense: Normal/Impaired Temperature sensation: Normal/Impaired

10 gram monofilament test: Normal/Impaired

20.Other systems:

**Investigations:**

FPG

2-h PG

HbA1c

CBC (MPV)

Fundal Photograph

Fasting Lipid Profile

Serum Creatinine

ECG

Urine Routine Examination

CRP

ACR

**Signature of the Researcher**

**Date**

**Appendix-II**

**Informed Written Consent:**

1. Title of the Study: **Association of Mean Platelet Volume (MPV) with Diabetic Retinopathy(DR) in Type- 2 Diabetis Mellitus (T2DM).**
2. Investigator’s Name: Dr. Md. Khasruzzaman Rony
3. Institution: Sylhet M.A.G. Osmani Medical College Hospital, Sylhet.
4. Do you know the type, purpose and procedure of this study? Yes / No.
5. Are you sure that you will not face any physical, psychological and social risk for this study? Yes / No.
6. Are you sure this study will not cause any physical or psychological harm? Yes / No.
7. Do you have freedom to refuse, participate or withdraw? Yes / No.
8. Do you loss any fundamental human rights due to participation in this study? Yes / No.
9. Do you feel that the confidentiality of your information will be maintained? Yes / No.
10. Do you know that you will get no remuneration or travel expenses due to participation in this study? Yes / No.

**Consent Form (English)**

Getting full information about the purpose, procedure and utility of this study, I give consent to participate in this study. I have not been influenced by anybody or groups or my fundamental human rights have not been violated due to participation in this study.

I am assured that confidentiality of all gathered information will be maintained and will be used for only study purpose and my personal information will not be disclosed to others.

My participation in this study is entirely voluntary. My decision whether or not participate will not prejudice my medical care. I have right to withdraw my consent and discontinue participation at any time without prejudice to me or affect on my medical care.

I will not get any renumeration due to participation in this study.

I am willingly giving signature to this consent form.

Signature of the participant

সম্মতি পত্র

এই গবেষণা কর্মের উদ্দেশ্য, পদ্ধতি ও উপযোগিতা সম্পর্কে পূর্ণ ধারণা পাইয়া এবং নীতিগত বৈশিষ্ট্য সমূহের প্রতি আমার সম্মতি প্রকাশ করিতেছি। গবেষণা কর্মে অংশগ্রহণের জন্য আমি কোন ব্যাক্তি বা গোষ্ঠীর দ্বারা প্রভাভিত হই নাই অথবা আমার মৌলিক মানবাধিকার ক্ষুণ্ণ হয় নাই। আমি নিশ্চিত হইয়াছি যে, এই গবেষণা থেকে সংগৃহীত তথ্যাবলি সম্পূর্ণ গোপন রাখা হইবে। এই তথ্যাবলি কেবলমাত্র গবেষণার কাজেই ব্যাবহার করা হুইবে। আমার ব্যাক্তিগত তথ্যাদি গবেষণাকারী ছাড়া অন্য কাঁরও নিকট প্রকাশ করা হইবেনা।

এই গবেষণায় আমার অংশগ্রহণ সম্পূর্ণ আমার ইচ্ছাধীন। আমি ইচ্ছা করিলে গবেষণায় অংশগ্রহণ নাও করিতে পারি, তাহাতে আমার চিকিৎসার তারতম্য হইবেনা। যে কোন মুহূর্তে আমি আমার সম্মতি প্রত্যাহার করিবার অধিকার রাখি। আমার এই প্রত্যাহার আমার চিকিৎসার উপর কোনরূপ প্রভাব ফেলিবেনা। অতএব, যথাযথ পর্যালোচনা সাপেক্ষে আমি স্বপ্রণোদিত হইয়া এই সম্মতিপত্রে স্বাক্ষর করিতেছি।

অংশগ্রহণকারীর স্বাক্ষর / বাম বৃদ্ধাঙ্গুলির ছাপ

সাক্ষীর স্বাক্ষর / বাম বৃদ্ধাঙ্গুলির ছাপ গবেষকের স্বাক্ষর ও তারিখ