



CORRELATION BETWEEN HEMATOLOGICAL PARAMETERS AND CARDIO METABOLIC RISK FACTORS: REPORT OF A STUDY AMONG ETHNIC TRIBAL WOMEN OF TRIPURA, INDIA.

MS. PURNAJITA SEN², MR. SANDIP DAS² AND DR. DIPAYAN CHOUDHURI^{1*}

¹Associate Professor, Department of Human Physiology, Tripura University (A Central University) Suryamaninagar, Agartala, Tripura – 799022, India

²Research Scholar, Department of Human Physiology, Tripura University (A Central University) Suryamaninagar, Agartala, Tripura – 799022, India

ABSTRACT

To examine the association between various hematological parameters and components of cardio metabolic risk factors among women from an ethnic tribal community of Tripura, India. Participants were 356 (190 pre-menopausal and 166 post-menopausal) women. Cardio metabolic risk of the subject was evaluated according to consensus statement for diagnosis of general obesity, abdominal obesity and metabolic syndrome for Asian Indians. Hematological parameters like red blood cell (RBC) count, white blood cell (WBC) count, Platelet count, count of neutrophil, lymphocytes, hemoglobin (Hb) concentration, hematocrit (HCT), mean corpuscular volume (MCV), mean corpuscular hemoglobin (MCH), red-cell distribution width (RDW-CV) of the subject were evaluated in a hematological analyzer. Hb showed significantly positive correlation with waist circumference (WC) of the subject. Platelet count, neutrophil count, HCT and MCH showed significantly positive correlation with systolic blood pressure (SBP). While, lymphocyte and RDW-CV showed significantly negative correlation with SBP. Platelet count and Hb concentration showed significantly positive correlation with diastolic blood pressure (DBP). Total WBC, Hb, MCV and MCH showed significantly positive correlation with triglyceride (TG) level. Total WBC showed significantly negative correlation with high density lipoprotein (HDL-C). While, platelet count showed significantly positive correlation with fasting blood sugar (FBS). Our study findings revealed that various hematological parameters are associated with number of cardio metabolic risk factors and can be used as an indicator for the early detection of individuals at risk for future development of cardiovascular disease.

KEYWORDS: SBP, DBP, TG, WC, Hb,.



DR. DIPAYAN CHOUDHURI

Associate Professor, Department of Human Physiology, Tripura University
A Central University) Suryamaninagar, Agartala, Tripura – 799022, India

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INTRODUCTION

Chronic non communicable diseases in particular cardiovascular disease and various metabolic disorders are increasingly becoming significant causes of morbidity and mortality in developing countries¹. World Health Organization projected by the year 2015, non communicable diseases will account for over 70% of all deaths globally with 80% of deaths occurring in developing countries². Rapid urbanization, changing lifestyle, socio cultural factors, poverty and poor maternal, foetal and infant nutrition form the basis of the development various non- communicable diseases³. Various data showed that women are increasingly becoming susceptible to various non-communicable diseases including cardio metabolic disorders⁴. Physiological and hormonal parameters in women might act as an additional risk factor for such diseases⁵. Recently, it has been identified that various hematological parameters show correlation with components of cardio metabolic risk in different groups of population. Hematological status is recorded during routine evaluation of health status of a subject. It is very convenient and an inexpensive investigative procedure⁶. In worldwide studies, investigators have reported that hematological parameters commonly obtained from routine clinical examinations may provide important information indicative of increased risk for cardio metabolic disorders. Some of them provide evidence that hematological parameters may be used in early detection and evaluation of cardiovascular disease prevention and control programs. Investigators have reported that increased hematological parameters (i.e., hemoglobin, hematocrit, platelet counts, red blood cell (RBC), and white blood cell (WBC counts) are associated with cardio metabolic risk factors.^{7,8} To our knowledge, no previous studies have investigated the relationship between hematological parameters and cardio metabolic risk components exclusively in women, specially belonging to an ethnic tribal populations. It is thus of interest to assess the relationship between hematological parameters and cardio metabolic risk components among women of a tribal community of Tripura, a North eastern state of India. Such information could be useful for cheap, highly dependable and accurate, routinely collected clinical hematological parameters for the early diagnosis of individuals at the risk for cardio metabolic disorders.

MATERIALS AND METHODS

Study Design

The study was conducted as a cross sectional study among three hundred and fifty six (356) women recruited randomly from a mixed population of young and old women ranging from 25-65 years of age. One hundred and ninety (190) among them were premenopausal (age 25-45 years) and one hundred and sixty six (166) were post menopausal (age 45-65 years) women. The participation to the study was completely on voluntary basis and informed consent was obtained from each participating subject after explain the purpose of the study to each of them in the language they understand. The calculated sample size for the study was three hundred and twenty three (323), taking 30%

prevalence with 95% of confidence interval and absolute precision of 5%.⁹ All the subjects were interviewed about their marital status, history of menstrual cycle and number of children. Subjects having fever for the past few days, history of any malignancy, thalasaemia, renal disease, jaundice, autoimmune disease, thrombocytopenia and subjects who donated blood within few months, clinically confirmed pregnancy and the subjects having any cardio metabolic disorder were excluded from the study. A questionnaire was formulated for the purpose. The age of the subject was recorded as mentioned by the subject.

Ethical Clearance

Ethical clearance for the study was obtained from Institutional Human Ethical Committee of Tripura University.

Experimental procedures

Initially, all the eligible subjects were evaluate for various anthropometric parameters following standard procedure¹⁰. Weight of the subject was measured by using weighing machine (Libra R, UK) with subject standing erect on the machine without shoes and in normal clothing. Height was measured using a stadiometer (Bio+Plus (R). S.NO-51392) with subject standing erect without any foot wear. Waist circumference was measured by positioning the measuring tap between coastal margin and iliac crest of the subject. Body mass index (BMI) was calculated using the standard expression: $BMI = \text{weight(kg)} / \text{height}^2 \text{ (m)}$. Waist to hip ratio (WHR), waist to height ratio (WHtR) were calculated by using formula. Blood pressure of the subject was recorded in supine position by using aneroid sphygmomanometer (Brand/ Model-Doctor Japan: Life line). Both systolic and diastolic pressures were recorded. Mean pressure and pulse pressure were calculated. ECG of the subject was recorded by a ECG Machine (Make-BPL, Model-Cardiart 9108 SI.No-DURB3C1004). About 10 ml non heparinised venous blood samples were collected after an overnight fast for biochemical and hematological analysis. The Blood Glucose level was estimated by using Digilabauto colorimeter. Serum total cholesterol, HDL cholesterol and triglyceride were estimated by using commercially available kit in a full auto analyzer (Erba - EM 200). The full blood count (FBC) was done at XS-800i (Sysmex, Kobe, Japan) for the following parameters Haemoglobin (Hb), Red blood count (RBC) and RBC indices including Mean Corpuscular Volume (MCV), Mean Corpuscular Haemoglobin (MCH), Mean Corpuscular Haemoglobin Concentration (MCHC) and hematocrit (HCT) or packed cell volume (PCV). Cardio metabolic risk of the subject was evaluated according to consensus statement for diagnosis of general obesity, abdominal obesity and metabolic syndrome for Asian Indians according to Joint Interim Statement of the International Diabetes Federation Task Force on Epidemiology and Prevention; National Heart, Lung, and Blood Institute; American Heart Association; World Heart Federation; International Atherosclerosis Society; and International Association for the Study of Obesity.¹¹ As per their consensus statements, women having three or more out of following five cardiovascular risk factors were identified as having cardio metabolic syndrome. The risk factors are:

- Increased waist circumference ≥ 80 cm.
- Hypertriglyceridemia ≥ 150 mg/dl (1.7 mmol/l)
- Low HDL < 50 mg/dl (1.3 mmol/l)
- Elevated blood pressure $\geq 130/85$ mmHg/Elevated blood sugar ≥ 100 mg/dl (6.1 mmol/L)

STATISTICAL ANALYSIS

The statistical analyses was performed using the PC version of SPSS statistical software (SPSS 20, IBM, Armonk, New York, USA). A *P* value (significance) of <0.05 is deemed statistically significant. A significance of .000 should be read as $P < .0001$ (very highly significant) as the software can detect significance up to 3 decimal points only. Parameters were expressed as

Mean \pm SD and percentage. Difference between groups were examined by unpaired 't' test. Pearson's correlation analysis was performed to establish relation between various obesity, glycemic, hematological markers and metabolic risk factors.

RESULT

The base line anthropometric characteristics of in pre and postmenopausal women with and without cardio metabolic risk factors are presented in Table - I. All the parameters except BMI varies significantly between the pre and post menopausal women with or without cardio metabolic risk.

Table 1
Base line characteristics of the anthropometric parameters in pre and postmenopausal Tripuri women with and without cardio metabolic risk factors.

Parameters	Total subject (356)	Postmenopausal women with cardio metabolic risk (61)	Postmenopausal women without cardio metabolic risk (105)	Premenopausal women with cardio metabolic risk (36)	Premenopausal women without cardio metabolic risk (154)
Age (yrs)	43.84 \pm 11.89	56.14 \pm 5.42	53.81 \pm 6.11*	37.83 \pm 5.90	33.58 \pm 6.36***
BMI (kg/m ²)	22.45 \pm 1.51	23.01 \pm 1.2	22.66 \pm 1.38 [#]	22.41 \pm 1.69	22.1 \pm 1.59 [#]
WC(cm)	79.33 \pm 3.94	82.43 \pm 4.21	78.20 \pm 3.62***	82.27 \pm 4.45	78.20 \pm 2.74***
WHR	0.76 \pm 0.07	0.80 \pm 0.08	0.75 \pm 0.06***	0.81 \pm 0.06	0.75 \pm 0.06***
WHtR	0.52 \pm 0.03	0.54 \pm 0.03	0.51 \pm 0.04***	0.53 \pm 0.03	0.52 \pm 0.03**

*BMI – Body mass index, WC- Waist circumference, WHR- Waist-hip ratio, WHtR- Waist-height ratio. (Values are in Mean \pm SD; * $p < 0.05$, ** $p < 0.01$, *** $p < 0.001$, # $p = NS$)*

The blood pressure, fasting blood glucose and lipid profile of pre and postmenopausal women with and without cardio metabolic risk factors are presented in Table - II. All the parameters, except HDL-C showed

significantly higher values in subjects with cardio metabolic risk both in pre and post menopausal women. HDL-C levels were significantly less among both pre and post menopausal women with cardio metabolic risk.

Table II
Base line characteristics of blood pressure, fasting blood glucose and lipid profile of the Tripuri subjects.

Parameters	Total subject (356)	Postmenopausal women with cardio metabolic risk (61)	Postmenopausal women without cardio metabolic risk (105)	Premenopausal women with cardio metabolic risk (36)	Premenopausal women without cardio metabolic risk (154)
SBP (mmHg)	123.53 \pm 6.35	126.88 \pm 5.63	123.80 \pm 5.43**	126.66 \pm 5.85	121.29 \pm 6.43***
DBP(mmHg)	81.61 \pm 7.16	85.65 \pm 7.49	80.14 \pm 6.10***	86.80 \pm 6.34	79.80 \pm 6.71***
FBS (mg/dl)	95.52 \pm 31.40	116.83 \pm 37.98	97.53 \pm 36.60**	111.11 \pm 27.67	82.06 \pm 14.60***
TG (mg/dl)	136.87 \pm 46.10	167.50 \pm 51.59	143.27 \pm 44.87**	170.83 \pm 34.72	112.43 \pm 31.12***
HDL-C (mg/dl)	55.79 \pm 19.17	41.67 \pm 15.84	56.18 \pm 20.59**	47.14 \pm 15.65	63.13 \pm 16.08***
LDL-C(mg/dl)	99.31 \pm 57.12	103.39 \pm 61.55	104.89 \pm 73.02 [#]	101.46 \pm 63.16	93.38 \pm 38.52 [#]
VLDL-C(mg/dl)	29.30 \pm 13.37	38.95 \pm 17.10	31.73 \pm 13.36**	38.82 \pm 9.10	21.59 \pm 6.11***
TC(mg/dl)	200.05 \pm 67.95	199.16 \pm 72.94	205.04 \pm 89.22 [#]	231.38 \pm 77.32	189.67 \pm 38.63***

*SBP- Systolic blood pressure, DBP-Diastolic blood pressure, FBS-Fasting blood sugar, TG-Triglyceride, HDL-C – High density lipoprotein- Cholesterol, LDL-C-Low density lipoprotein, VLDL-C-Very Low density lipoprotein, TC- Total cholesterol (Values are in Mean \pm SD; * $p < 0.05$, ** $p < 0.01$, *** $p < 0.001$, # $p = NS$)*

Table III represents the details of haematological parameters evaluated in the study population. It has been found that except total lymphocyte count and

RDW-CV all the haematological parameters are significantly high in post menopausal women in comparison to premenopausal women.

Table III
The details of Haematological parameters evaluated in pre and post menopausal women from Tripuri community.

Parameters	Total subject(356)	Premenopausal women (190)	Postmenopausal women(166)	P - Value
Total RBC count (millions/mm ³)	3.84±0.73	3.79±0.72	3.89±0.74	0.19 [#]
Total WBC count (thousand/mm ³)	8.36±2.27	7.79±2.35	9.01±2.00	0.0001***
Platelet count (lakhs/mm ³)	193.91±34.31	186.58±30.57	202.30±36.45	0.0001***
Neutrophil(%)	68.25±13.60	64.77±13.74	72.23±12.33	0.0001***
Lymphocyte(%)	25.55±12.14	28.22±12.59	22.50±10.85	0.0001***
Haemoglobin(gm%)	11.76±1.95	11.45±1.97	11.93±2.27	0.03*
HCT(%)	33.15±4.19	32.82±3.37	33.53±4.94	0.11 [#]
MCV(femtoliters/cell)	76.16±8.63	74.50±7.77	78.05±9.19	0.0001***
MCH(picograms/cell)	25.91±2.88	25.42±2.57	26.46±3.12	0.001**
RDW-CV(%)	14.18±1.22	14.34±1.30	14.01±1.09	0.01*

*RBC- Red blood cell, WBC- White blood cell, HCT- hematocrit , MCV-Mean corpuscular volume, MCH- Mean corpuscular hemoglobin, RDW-CV- Red blood cell distribution width. (Values are in Mean ± SD; *p<0.05, **p<0.01, ***p<0.001, #p=NS)*

The correlation between traditional metabolic risk factors along with haematological parameters are represented in Table-IV. Hb showed significantly positive correlation with WC. Platelet count, count of neutrophyl, HCT and MCH showed significantly positive correlation with SBP. While, Lymphocyte and RDW-CV showed significantly

negative correlation with SBP. Platelet count and Hb showed significantly positive correlation with DBP. Total WBC, Hb, MCV and MCH showed significantly positive correlation with TG. Total WBC showed significantly negative correlation with HDL-C. While, Platelet count showed significantly positive correlation with FBS.

Table IV
Correlations between cardio metabolic risk factors along with hematological parameters in total study population

HematologicalParameters	WC		SBP		DBP		TG		HDL-C		FBS	
	r	p	r	p	r	p	r	p	r	p	r	p
TOTAL RBCCOUNT	.084	.113	.048	.366	.091	.088	.063	.237	.083	.118	.060	.258
TOTAL WBC COUNT	.015	.772	.011	.830	-.026	.623	.141**	.008	-.104*	.049	.055	.297
PLT COUNT	-.030	.578	.225**	.000	.161**	.002	-.027	.611	-.008	.875	.165**	.002
NEUTROPHYL COUNT	-.043	.421	.121*	.022	-.062	.246	.069	.191	.010	.853	.039	.464
LYMPHOCYTE COUNT	.040	.456	-.122*	.021	.052	.331	-.030	.574	.007	.901	-.011	.836
HB	.250**	.000	.087	.100	.166**	.002	.210**	.000	-.003	.959	.057	.285
HCT	-.043	.420	.110*	.038	.087	.103	.035	.510	.012	.826	.000	.995
MCV	-.088	.098	.077	.145	.005	.919	.136*	.010	-.051	.341	.047	.374
MCH	-.028	.604	.132*	.012	.082	.121	.147**	.006	-.075	.158	.071	.180
RDW-CV	-.021	.695	-.121*	.022	-.039	.466	-.066	.213	.011	.829	-.086	.104

*WC- Waist circumference, SBP- Systolic blood pressure, DBP-Diastolic blood pressure, FBS-Fasting blood sugar, TG-Triglyceride, HDL-C – High density lipoprotein- Cholesterol, Hb-Hemoglobin concentration.RBC- Red blood cell, WBC- White blood cell, HCT- hematocrit , MCV-Mean corpuscular volume, MCH- Mean corpuscular hemoglobin, RDW-CV- Red blood cell distribution width. (*Correlation (2-tailed) is significant at the 0.05 level ** Correlation (2-tailed) is significant at the 0.01 level*

DISCUSSION

Evidence revealed that tribal populations are affected by various social, economic and developmental constraints that potentially expose them to high rates of malnutrition and health problems which is correlated with incidence of different non-communicable diseases among them. One of the major non-communicable diseases that affect the tribal population, especially the women, is nutritional anaemia. This is particularly serious in view of the fact that both rural and tribal women have poor hygiene practice, nutritional deficiency and heavy workload that affect their psychological and physical health.^{12,13} Recently, various studies showed that cardio metabolic risk factors are one of the major health problem among women from indigenous tribal population.^{14,15} We assessed both cardio metabolic risk profile and hematological profile of our study subjected and evaluated their association. We found many hematological parameters were positively associated with components of metabolic risk factors in both pre and post menopausal women. A study performed in Tobago reported that RBC count, Hgb concentration,

and Hct levels in patients with type 2 diabetes mellitus were lower than the control group.¹⁶ The possible hypothesis for this might be that chronic hyperglycemia caused nonenzymatic glycosylation of RBC membrane proteins that led to accelerated aging of RBCs. Similar study on middle-aged and elderly Chinese population in Taiwan also reported a reduced RBC count in patients with insulin resistance (IR). Another study observed that diabetic patients were prone to anemia due to reduced kidney functions and decreased production of erythropoietin hormone, which eventually led to decreased RBC count in the body.¹⁷ In the present study, we observed that both waist circumference (WC) and triglyceride (TG) were associated with Hb. This finding was consistent with the results of other major studies conducted in population of different age groups.¹⁸ The relationship between WC and Hb is a well known fact. It is well known that increased WC can cause insulin resistance (IR), which is related to low grade inflammation.¹⁹ This inflammation can elevate Hb level. Thus, increased WC can eventually have an effect on the level of Hb concentration. At the same time, low-grade inflammation is also a mediator for the correlation

between TG and Hb. The postprandial hypertriglyceridemia could cause the increase of ICAM-1 and VCAM-1, which are markers of chronic inflammation.²⁰ According to biological pathways, several hematological changes affecting the red blood cells (RBCs), white blood cells (WBCs), and the coagulation factors are shown to be directly associated with cardio metabolic risk factors.²¹ Systematic review and meta-analysis of cross-sectional studies have shown that the number of peripheral WBCs such as basophils, eosinophils, and neutrophils increased, with no change in the number of monocytes in patients with type 2 diabetes melitus.²² Hyperglycemia results in impairments in cellular metabolism due increased production of reactive oxygen species (ROS) and non-enzymatic glycation of many macromolecules, which eventually lead to changes in cellular structure and function, and formation of advanced glycation end products (AGEs). The formation of AGEs enhances metabolic impairments and also increases reactive oxygen species production via interaction with the specific receptor for AGE (RAGE).²³ This results changes in structure and biophysical properties of the basement membrane which further causes changes in permeability and vasodilatation of blood vessels.²³ A study suggested that altered platelet morphology and function can be reflected as a factor for risk of microvascular and macrovascular diseases.²⁴ Several studies have reported that elevated platelet reactivation in patients with diabetes may confer less cardiovascular protection with antiplatelet therapy, particularly aspirin.²⁵ It has already been reported that insulin resistance (IR) and hyperinsulinemia are associated with the stimulation of erythroid progenitors and increased levels of inflammatory markers.²⁶ Patel et.al. from their study on subjects with metabolic syndrome showed that platelet volume indices (PVI) may be used as a better predictor for acute complication in patients with metabolic syndrome.²⁷ Epidemiological study has demonstrated a close relationship between the WBC count and components of metabolic syndrome.²⁸ These abnormalities have been shown to markedly elevate blood viscosity that unfavorably affects the microcirculation, which ultimately leads to microangiopathy.²⁹ Studies showed that higher WBC count, as one of the major components of inflammatory process, contributes to atherosclerotic progression and

cardiovascular diseases.²⁸ Hematological indices are important indicators for the evaluation of variations in size, number, and maturity of different blood cells. They are important for the assessment and management of subjects having cardio metabolic risk. In hematological perspective, it has been observed that there is a significant difference in white blood cell level in metabolic risk factor subjects. This is in agreement with the study conducted by Vichinsartvichai P, Siriwan S.³⁰ In spite of unascertained aetiology of cardio metabolic risk, the chronic systemic inflammatory state seems to be the pivotal mechanism underlying the development of cardio metabolic risk through complex pathways such as monocyte chemoattractant protein-1 (MCP-1), tumor necrosis factor α (TNF- α) and interleukin (IL-6), serine phosphorylation of insulin receptor substrate-1 (IRS-1) increment through activation of c-Jun N-terminal kinase (JNK) and I κ B kinase (IKK), and toll-like receptor (TLR4) signaling pathway.³¹ White blood cell (WBC) count is a routinely measured marker of systemic inflammation and elevated WBC count or its subtype is intimately linked to the prevalence of cardio metabolic risk in previous population-based studies.³² Other hematologic parameters including platelet count and hemoglobin are also associated with cardio metabolic risk and its components in some studies.³³ Our findings suggested that hematological parameters are potentially important biological markers of cardio metabolic risk. Inferences can be elevated by future studies that might aim to identify the relationships between incident cardio metabolic cases and hematologic parameters.

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CONFLICT OF INTEREST

Conflict of interest declared none.

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Reviewers of this article

Dr S. Vijayaram

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Prof. Srawan Kumar G.Y

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Pharmaceutical Sciences, Sattenapalli,
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