VOLUME-8, ISSUE-3, MARCH-2019 • PRINT ISSN No 2277 - 8160

Original Research Paper

Physiology

ALTERATION OF RED CELL COUNT IN CHRONIC MENTAL STRESS

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ABSTRACT

Stress causes deviation from homeostasis. Originally designed to fight adversities of major and minor kinds, it's now becoming a major health hazard due to increased activation of the stress response. Alteration in lifestyles is one of the major factors responsible for rise in stress. Job stress is a kind of chronic mental stress which can cause physical changes in the body like altered haematological parameters. This study was done to detect any change of red cell count due to chronic mental stress. It is observed that chronic mental stress is associated with rise in RBC count, for which excess cortisol and prolonged activation of sympathetic nervous system play a great role. Rise of red cell count is associated with increased blood viscosity which independent of platelet count can predispose to thrombi formation and CVS diseases.

KEYWORDS : Stress, Red Cell Count, Cortisol, Stress Polycythaemia.

INTRODUCION:

Stress is defined as any change in the environment that changes or threatens to change an existing optimal steady state (**homeostasis**).[1] Most of the stresses activate processes at the molecular, cellular, or systemic level that tend to restore the previous homeostatic state.[1]

It was originally designed to help face challenges, but continuation of this response is detrimental to health. Increased prevalence of stress is seen nowadays due to alteration in lifestyle.

Stress can be categorized into various types such as: Acute/ Chronic; Physical/ Mental etc.

TYPES OF STRESS:

(i) **Acute stress**: Response/reaction to immediate threat, real or perceived even subconsciously or falsely as a danger[2].

(ii) **Chronic stress**: Stress of unrelenting demands and pressures for seemingly interminable periods of time.[2] An important characteristic of distress is that the physiologic response either persists long after the stressor has ceased or is activated repeatedly to result in an overall integrated increase in exposure of the organism to stress hormones. It is recognized to be damaging to the body in the long run .[3]

Chronic stressors, usually pervade a person's life, forcing him or her to restructure his or her identity or social roles. Another feature of chronic stressors is their

stability—the person either does not know whether or when the challenge will end or can be certain that it will never end.[4]

Thus, acute stress has been defined as stress that lasts for a period of minutes to hours and chronic stress as stress that persists for several hours per day for weeks or months[5].

PHYSICAL STRESS: It is the human body's response to physical pressures such as work, illness, exercise etc.[6]

MENTAL STRESS: A state of mental arousal, mental tension and worry[7,8]. Eg: job stress. Job strain is defined as a combination of low control and high demands at work.[9]

Occupational stress (OS) is experienced when an individual is exposed to an overload of stressors originating wholly (or largely) from the occupational environment.[10]

STRESSOR:

A chemical or biological agent, environmental condition, external stimulus or event which causes stress to an organism.[11] or acts as an external or internal challenger to homeostasis.[12] It causes release of stress hormones.[13]

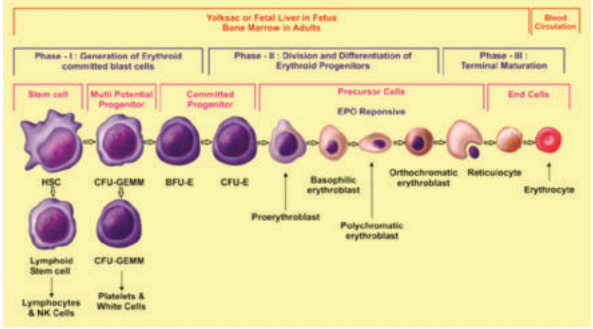
The major pathways activated by stressors are the hypothalamic-pituitary-adrenal (HPA) axis and the autonomic nervous system (ANS)[14]

RED BLOOD CELLS: Cellular component of blood.

Normal values of Red Blood cell (RBC) count: In healthy men, the average number of RBCs per cubic millimeter is 5,200,000 (±300,000); in women, it is 4,700,000 (±300,000).[23]

RBC production is highly dependant on a hormone – **Erythr op oietin (EPO),** which is produced by the kidney and to a lesser extent by the liver. This cytokine supports erythropoiesis or red cell development. Its production is mainly triggered by Hypoxia, which increases the abundance of the **α subunit of the hypoxia-inducible factor 1 (HIF-1α),** enhancing production of erythropoietin mRNA. Although EPO is not absolutely required for early commitment of progenitor cells to the erythroid lineage, it is essential for the differentiation of burst-forming unit–erythroid cells (BFU-E) to CFU-E or proerythroblasts (also known as pronorm oblasts), which still lack hemoglobin. The further maturation of cells downstream of proerythroblasts does not require EPO. Hemoglobin first appears at the stage of polychromatic erythroblasts and is clearly evident in orthochromatic erythroblasts. The subsequent exocytosis of the nucleus produces reticulocytes whereas the loss of ribosomes and mitochondria yields mature erythrocytes, which enter the circulation. The mature erythrocyte has a life span of ~120 days. Immature reticulocytes may also appear in the circulation when erythropoiesis is heavily activated.[24]

FIGURE 1: ERYTHROPOEISIS – formation of mature RBC from Stem Cells.[25]



AIMS AND OBJECTIVES:

To study the effect of chronic mental stress on red cell count.

METHODOLOGY:

(I)MATERIALS AND METHODS: Clearance for this study was given by the Institutional Ethics Committee, Gandhi Medical College, Secunderabad, Telangana. A letter of informed consent was taken from the volunteers.

(II)STUDY POPULATION: 50 individuals, comprising of 28 males and 22 females, aged 20-30 years working in IT companies.

(III) Format for collection of personal information was given to the volunteers.

(IV) General Physical examination was done.

PARAMETERS ASSESSED:

1. **Red cell count** - using an Automated analyser
2. **DASS SCORE** –using a Questionnaire

2 blood samples collected from each subject under aseptic precautions at an **interval of about 6 months**.

Collection of 1st sample – Subjects had *Newly joined* their respective organizations. It acted as a baseline to ensure that the haematological parameter is within normal physiological range.

Collection of 2nd sample – after stress exposure for a period of 6 months.

The subjects did not have night shifts for 1 month prior to 2nd blood test, in order to prevent altered sleep schedule acting as an added, independent factor which can affect the haematological parameter. Mental stress is more of a subjective phenomenon with each volunteer perceiving different amounts of stress for the same task. Hence **DASS -42 questionnaire (Depression, Anxiety and Stress scale)** was provided to each subject. They were assessed only for the stress scale.[15] The Stress scale (items) is sensitive to levels of chronic non-specific arousal. It assesses difficulty relaxing, nervous arousal, and being easily upset/agitated, irritable/over-reactive and impatient.[15] The Stress scale, originally labelled "tension/stress", measures a syndrome that is factorially distinct from depression and anxiety, characterised by nervous tension, difficulty relaxing and irritability. DASS scale can be used to measure stress over a **varying time period which can be chosen by the examiner**[16]. Even though DASS has 3 scales, omitting a scale won't have any noticeable effect on scores for the remaining scales. Hence in this study, only Stress Scale was used[16]. They were graded as having no/mild/ moderate/ severe stress, according to the DASS score.

None of the subjects in either group reported any cigarette smoking or alcohol intake. Each subject reported a sleep duration of 7 or more hours per day.

DAS S		***Name:***	***Date:***
Please read each statement and circle a number 0, 1, 2 or 3 which indicates how much the statement applied to you ***over the past 6 months***. There are no right or wrong answers. Do not spend too much time on any statement.			
The rating scale is as follows: **0** Did not apply to me at all **1** Applied to me to some degree, or some of the time **2** Applied to me to a considerable degree, or a good part of time **3** Applied to me very much, or most of the time			
1	•	I found myself getting upset by quite trivial things	0 1 2 3
6	•	I tended to over-react to situations	0 1 2 3
8	•	I found it difficult to relax	0 1 2 3
11	•	I found myself getting upset rather easily	0 1 2 3
12	•	I felt that I was using a lot of nervous energy	0 1 2 3
14	•	I found myself getting impatient when I was delayed in any way (eg, lifts, traffic lights, being kept waiting)	0 1 2 3
18	•	I felt that I was rather touchy	0 1 2 3
22	•	I found it hard to wind down	0 1 2 3
27	•	I found that I was very irritable	0 1 2 3
29	•	I found it hard to calm down after something upset me	0 1 2 3
32	•	I found it difficult to tolerate interruptions to what I was doing	0 1 2 3
33	•	I was in a state of nervous tension	0 1 2 3
35	•	I was intolerant of anything that kept me from getting on with what I was doing	0 1 2 3
	•	I found myself getting agitated	0 1 2 3

CATEGORY OF STRESS	DASS SCORE
No Stress	0-14
Mild	15-18
Moderate	19-25
Severe	26-33
Very Severe	34+

INCLUSION AND EXCLUSION CRITERIA:

Criteria for inclusion was apparently healthy volunteers who are not having any signs of chronic disease.

Criteria for exclusion was:

(i) Any chronic disease(s), anaemia, recent major trauma or surgeries.

(ii) Any intake of medication for the above mentioned conditions – eg: haematinics.

STATISTICAL ANALYSIS:

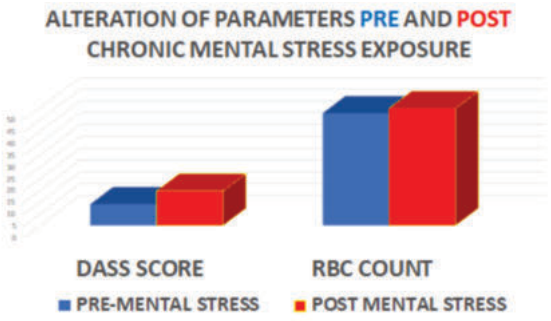
Student 't' test was done. Analysis was done using Graphpad Instat Software.

RESULTS:

TABLE 1: TABLE SHOWING RBC COUNT AND DASS SCORE PRE AND POST EXPOSURE TO CHRONIC MENTAL STRESS.

PARAMETER	PRE-MENTAL STRESS	POST MENTAL STRESS	p VALUE	LEVEL OF SIGNIFICANCE
DASS SCORE (MEAN + SD)	8.687 + 1.988	14.866 + 1.912	<0.001	EXTREMELY SIGNIFICANT
RBC COUNT (in millions/cu.mm) (MEAN + SD)	4.67 + 1.014	4.962 + 0.485	0.0151	SIGNIFICANT

GRAPH 1: GRAPH SHOWING RBC COUNT AND DASS SCORE PRE AND POST EXPOSURE TO CHRONIC MENTAL STRESS



NOTE: RBC count divided by a million in order to make a comparitive graph. Actual values present in Table.

DISCUSSION:

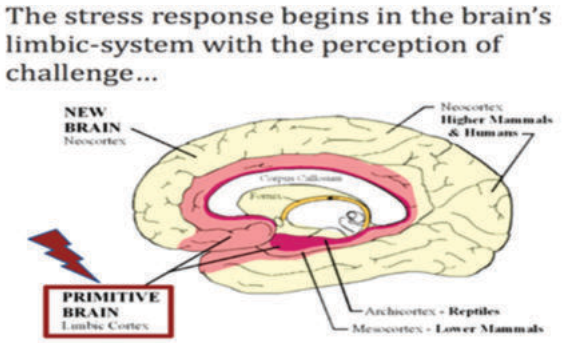
This study intended to compare and detect any alteration of red cell count in individuals post exposure to chronic mental stress.

As Mental stress is more of a subjective perception, DASS questionnaire measuring Stress scale was given to the subjects. DASS scores at the **onset of study** showed scores which translated to **NO STRESS**. Following this blood samples were taken, which showed RBC count to be within physiological limits. These parameters served as a baseline as well as to rule out any aberrations beyond the normal range.

Significant rise in RBC count in post Mental stress exposure was seen with a **p value of 0.0151**, which is significant. 16% of males and 16% of females show an increase above physiological limits, whereas the rest of the group was within normal range, although they showed a rise from the baseline pre exposure values. The difference in the rise of RBC count between males and females was insignificant. (p = 0.054).

Extremely Significant rise in Stress scale score of DASS score post exposure was also seen, with a p value of less than 0.0001.
Stress evokes a stress response which causes multiple changes in the body in different steps.

Figure 2: PERCEPTION OF A CHALLENGE OR STRESS BY LIMBIC SYSTEM[17].

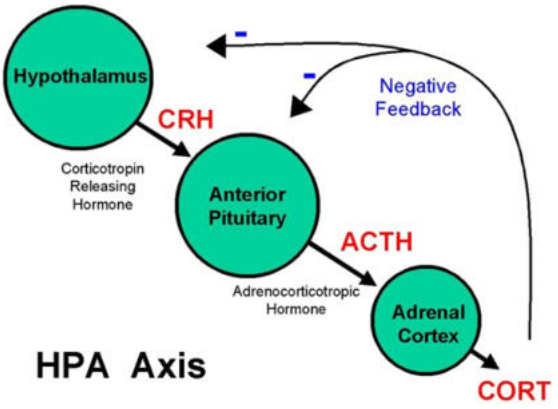


Mental stress causes rise of ACTH secretion too.

Increased activity in the limbic system, especially in the region of the **amygdala and hippocampus**, both of which then transmit signals to the **hypothalamus**.

Hypothalamus causes release of Corticotrophin Release Hormone (CRH), which in turn acts on Anterior Pituitary Gland to release Anterior Corticotrophic Hormone (ACTH). ACTH acts on the adrenal glands to release Cortisol.

Figure 3: HPA AXIS SHOWING STRESS RESPONSE AND RELEASE OF VARIOUS HORMONES FROM VARIOUS GLANDS.[18]



ROLE OF ANS IN STRESS:

The ANS has two divisions, the sympathetic nervous system (SNS) and the parasympathetic nervous system (PNS). In response to stressors, the hypothalamus secretes corticotropin-releasing hormone which is released and acts on the noradrenergic centers in the brainstem and spinal cord[14].

The locus coeruleus of the brainstem sends direct projections to the sympathetic preganglionic neurons in the spinal cord and to the parasympathetic preganglionic neurons in the brainstem and the spinal cord. The activation of the SNS in turn stimulates the release of CRH by the hypothalamus, creating a positive bidirectional feedback loop[14].

Normally SNS is activated in stress while PNS is activated when the stress is decreased because the SNS and the PNS are highly coordinated to maintain physiological homeostasis. This balance is lost in conditions where stressful situations persist. The SNS continues to be activated without the normal counteraction of the PNS.[14]

There could be **2 factors responsible for rise in RBC count** due to stress:

1.STRESS POLYCYTHAEMIA: This is a relative polycythaemia, which could be due to a primary contraction of the vascular compartment[19]. It is secondary to exogenous or endogenous stress and is mediated via the sympathetic nervous system. This contraction is usually mediated by the increased adrenergic activity which reduces the circulatory capacitance volume.[19,20]

2.EXCESS CORTISOL:It causes **increased Erythropoeitin synthesis**[21]
Additionally, there is stimulation of the earliest Blast forming units – Erythroid (BFU-E) progenitors to undergo limited self-renewal, which increases formation of CFU-E cells > 20-fold[22]

Rise of RBC count leads to **increased blood viscosity** which in turn predisposes to thrombi formation, independent of platelet count.

Additionally stress itself is associated with endothelial dysfunction, and procoagulation changes.

All of them act as risk factors for thromboembolic phenomenon and Cardiovascular diseases.

CONCLUSION:

- Stress is a phenomenon which is universally experienced.
- Chronic mental stress causes significant rise of RBC count.
- Risk factor for CVS diseases in future.

- Control of stress levels by possible alterations in lifestyle, exercise, yoga etc..
- ***Regular health check up & testing of hematological parameters recommended.***

ACKNOWLEDGEMENTS:

- I offer my sincere thanks to my subjects, my guide Dr. D. Joya Rani, Prof & HOD, Department of Physiology, Govt. Medical College, Nizamabad, Telangana, Dr. Geetha, MD, Dr. Anitha, Dr. Rama Devi, Dr. O. Padmini, Dr. Padma, Dr. Ganesh and my senior and junior colleagues for their cooperation and support.

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