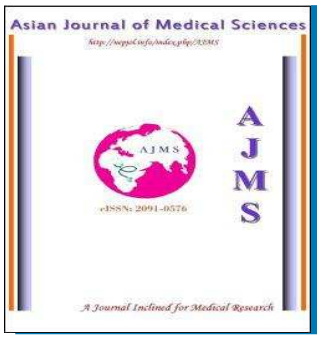

CAUSES AND RISK FACTORS FOR POST-TRAUMATIC STRESS DISORDER: THE IMPORTANCE OF RIGHT DIAGNOSIS AND TREATMENT

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ABSTRACT

Post-traumatic stress disorder (PTSD) is a serious debilitating syndrome with significant personal, social, and economic consequences. People with PTSD experience one or more major symptoms that include flashbacks and paranoia, difficulty in interpersonal relationships, and problems engaging in work and activities of daily living. In severe cases they can harm themselves or the others; but these events are preventable by appropriate therapies.

PTSD is a well-characterized serious psychological and behavioural abnormality that occurs after exposure to one or more acute severe stressful events. It often occurs among soldiers returning from battlefields and the civilian victims of war. However, it also occurs in non-war situations, such as terrorist attacks or serious accidents; sexual abuse, rape, or other violent acts; and school or workplace bullying, harassment, or retaliation. Nevertheless, the diagnosis of PTSD is made too infrequently, particularly in the post-conflict periods in developing countries. This is in part because of inadequate awareness but also due to limited resources and expertise.

Consequently, the resources for clinical care and research are diverted to other forms of behavioral issues, such as adjustment disorders. The treatment of PTSD needs to be well coordinated so that all stakeholders work synergistically using the resources necessary for the prolonged treatment and follow-ups. PTSD is under-diagnosed, and even misdiagnosed or mislabeled as depression or adjustment disorders. The failure to make a timely diagnosis or mislabeling of PTSD likely will harm victims and their families and may lead to negative outcomes, including suicide. The provision of appropriate, well organized, individualized, cost-effective treatment plans should alleviate PTSD symptoms and enable those with the disorder to return to their normal productive lives.

Key words: Neurons, psychiatry, homeostasis, structure-function, behavior, psychotherapy.

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"The diagnosis and management of PTSD in Asian Countries: Options and pitfalls"

INTRODUCTION

Post-traumatic stress disorder (PTSD) is a debilitating syndrome that leads to significant personal, social, and economic consequences.[1-4] Although many patients with PTSD experience acute stresses or grief reactions, others may develop sinister behavioral issues including, suicidal ideation.[5,6] PTSD affects not only direct victims of trauma, but also their families, observers, as well as direct and indirect participants in traumatic events. Contrary to popular belief, PTSD occurs in civilians in higher numbers than with the soldiers; in scenarios outside of war experiences.[7,8] In fact, those with PTSD who have not been in war situations outnumber by several-fold, post-war PTSD military victims.[9] Many studies have been conducted over the years about PTSD in war veterans, trauma victims, and other groups of people exposed to man-made or natural disasters.[10]

The understanding PTSD is incomplete, as is its pathophysiology.[11] Several studies have demonstrated a variety of disabilities associated with PTSD, including work-related impairments[12,13]; somatic complaints and medical illnesses[14,15]; poor quality of life [16]; negative body image[17]; impaired memory and intimacy [18]; increased burden to spouse, partners, or family[19]; partner abuse [20]; social dysfunction [21,22]; and suicidal tendency [13,23,24]. PTSD is a complex disorder that requires integrating cognitive, functional, and pharmacologic components effectively. However, there are other several common disorders that can coexists with PTSD; treatment of these should not be ignored in patients with the disorder.

Definition of PTSD:

Post-traumatic stress disorder is defined as a severe anxiety disorder that develops after exposure to one or more serious life events resulting in deep psychological trauma[25,30]. People with PTSD may experience paranoia or flashbacks and have difficulty engaging in interpersonal relationships and activities of daily living. The *Diagnostic and Statistical Manual of Mental Disorders* (DSM) diagnostic criteria of PTSD require that the symptoms last more than one month and cause significant impairment in social, occupational, or other areas of human behaviour. However, in the DSM-V, the PTSD has move from the class of anxiety disorders into a new class of trauma and stressor-related disorders.[31]

Diagnostic criteria for PTSD include re-experiencing the original trauma through flashbacks of memories and nightmares, avoidance of stimuli associated with the trauma, and the occurrence of increased behavioral disorders following the primary trauma.[26] Flashbacks or involuntary recurrences of unpleasant memories are a known psychological phenomenon[32] in which an individual has a sudden, powerful memory of a past encounter or experience.

Prevalence of PTSD:

The risk of developing PTSD is higher in women, especially in those with personal or family histories of childhood mental trauma, those exposed to more intense or enduring trauma,[33,34] or those who have had a major medical illness.[35,36] In primary care, the prevalence of PTSD thought to be between 7% and 10%.[37,38] These numbers may be underestimations, because patients may not volunteer correct diagnostic information about their PTSD and/or clinicians may not ask the right questions to clarify symptoms to make the right diagnosis.[36,37,39]

Asian perspective of PTSD

Due to the under diagnosis and under reporting, the incidence of PTSD is higher than what is reported among the wounded soldiers and civilians following exposure to major trauma or stresses.[7] Direct exposure to a major natural disaster, [40-42] such as 2004 tsunami may precipitate PTSD in all age categories.[43,44] The pattern of development of PTSD may be different, but exposure to a major traumatic event, torture,[23,45,46] war, [47,48] refugee status [49,50] or a terrorist attack among Asians leads to the development of a similar incidence of PTSD that is reported in the west.[51,52] While ethnic and cultural differences are present in the Asian subcontinent, [53,54] it is not uncommon for people to develop PTSD after a significant lag time after a major traumatic event.[55,56]

Complex aetiology of PTSD:

PTSD is a complex disease with a multi-factorial etiology. Proposed complex interactions leading to the precipitation of PTSD are illustrated in Figure 1, in a schematic way. Once fully established, PTSD often follows a chronic, unremitting course.[57,58] Even those with only partial symptoms have increased comorbidity,[59-61] physical and mental impairment,[62] and develop suicidal ideations.[63-65] The incidences of

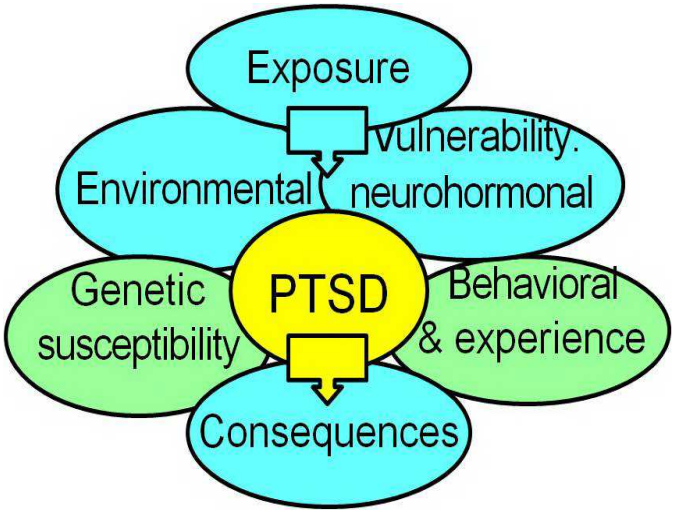

Figure1. The multi-factorial aetiology of PTSD is illustrated. Once the conditions are set with the exposure to deleterious inputs, changes that are associated with the neurohormonal system promote negative structural branch changes and the establishment of PTSD.

violence and substance abuse and substance dependence (primarily alcohol) are higher among those with PTSD compared to the general population. Soldiers and trauma-exposed civilians who experience PTSD also have higher rates of involvement with violent offenses and the criminal justice system.[66,67] In addition, the rescue workers including paramedics and ambulance personnel demonstrate a higher incidence of developing PTSD than the general population.[68,69] Those who has psychological disturbance or a psychiatric disorder prior to the exposure[32,53,70] are more likely have a higher incidence of PTSD including suicides.[23,46] Data also suggest that the pre-existing of familial psychopathology may increased the risk of traumatic exposure-induced PTSD.[71] Therefore, one need to be especially careful in selecting and, perhaps excluding those with preexisting psychological conditions sending to the frontline, as they likely to have a higher probability of developing PTSD following traumatic exposure. [32,71]

Patho-biological aspects of PTSD:

Post-traumatic stress disorders produce intense negative feelings of fear, distrust, helplessness, and horror in victims.[11] Although most studies of PTSD have been conducted in war veterans, several long-term studies have reported high incidences of PTSD among non-war trauma subjects.[72-74] Key precipitating events in non-war situations include life-threatening illnesses,[26] home-invasions, terrorist attacks[75] or serious accidents. Pathobiological point of view, individuals vulnerable for the development of PTSD may have dysregulation of the glucocorticoid-signalling pathway[82,83] (i.e., low base line levels of circulating cortisol and/or inability to increase cortisol levels appropriately, after stress or trauma -sub-threshold responses from the adrenal glands).[80] Development of simple but reliable procedures, to assess the vulnerability (prior to exposure to a major event or sending soldiers to the frontline) of a given person is vital, because not everyone exposed to trauma experiences PTSD.[84]

Many studies have confirmed that PTSD is associated with several comorbid psychiatric disorders.[85-91] In addition, patients with PTSD and major psychiatric disorders suffers from a variety of other disabilities.[59,92,93] Functional impairment in sub-threshold PTSD might be explained by the presence of disorders, as observed in dysthymia.[94,95] The identification of underlying susceptibility factor(s) may allow not only avoiding them getting exposure but also targeting of preventive intervention for individuals at high risk for PTSD.

Risk factors and causes of PTSD:

Some of the other recognized causes of PTSD include experiencing or witnessing serious physical,[86] emotional, or sexual abuse[26]; physical assault; sexual assault; major accidents or illnesses; drug addiction; and war situations, major natural or man-made disasters.[96,97] In addition, children and adults may experience PTSD symptoms after bullying by peers[98] or mugging [37,99,100] incidents. Research has also reported that about 25% of children exposed to significant violence can experience acute or delayed-onset PTSD.[100, 101] While lack of trust and resources could be associated with increased vulnerability, family and the community solidarity, sense of belonging, and confidence in services and the authorities may protective developing PTSD in exposed victims.[102]

In addition to trauma history at a young age, the war-zone stressors and atrocities, abuse, violence, and

perceived threat affect post-war resilience and recovery; other stressful life events and inadequate functional, family, or community and social support also may aggravate the existing situation or trigger PTSD.[103,104] In some patients, flashbacks and nightmares can be greater contributors to the biological and psychological dimensions of PTSD than is the event itself.[105] In susceptible people, most major traumatic exposure, event-associated memories becomes prominent and flashbacks may occur on frequent basis.[3] Combat exposure and the discomfort in disclosing exposure-experiences are also associated with an increased risks for developing PTSD.[106] Changes in chemical balances, structural changes in the brain,and the associated cascade of pathological neurohormonal changes likely to establish PTSD.[74]

Psychological and hormonal aspects of PTSD:

Chronic psychological stresses, irrespective of the underlying reason, negatively affect body systems, particularly the immune and the neuroendocrine systems.[107] Those who are vulnerable to develop or have developed PTSD secondary to major psychological or physical traumatic events usually have impaired endocrine glandular functions, at least temporarily. These include thyroid dysfunction, sustained elevation of adrenaline and noradrenalin, and a paradoxical suppression of corticosteroid and the glucocorticoid responses via its receptor abnormalities.[11,108]

Although the level of glucocorticoids is likely to be higher in the acute stressful situations, in people who are vulnerable to develop PTSD, it soon becomes suboptimal. This is one of the key mechanisms of the development and the sustenance of PTSD (Figure 2).

The fear response is a key element in PTSD. However, because of the chemical imbalances in the hypothalamic nuclei, the responses to fear become irrational in patients with PTSD. The amygdala is responsible for threat detection, and the conditioned and unconditioned fear responses that carried out as a response to real or perceived threats. The activity of the medial prefrontal cortex, a part of the amygdala, can inhibit the conditioned fear responses during trauma [78]and thereby negatively influence the hypothalamic-pituitary axis (HPA).

Over-activation of the locus coeruleus–noradrenergic system is also implicated in the abnormal retention and over-consolidation of memories that occur after a major trauma that is common in patients with PTSD.[109] These associations and abnormal HPA responses are likely to initiate the development and sustenance of PTSD.

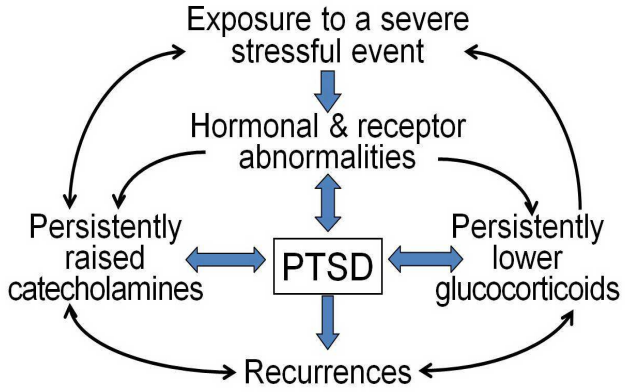

Figure2. Illustrates the potential mechanisms that precipitate PTSD. After exposure to a severe stressful situation, those who are likely to develop PTSD will continue to have sustained low levels of the circulatory glucocorticoids. These suboptimal serum glucocorticoid levels and sustained elevation of norepinephrine and epinephrine levels presumably initiate a cascade of other neurohormonal abnormalities and forces a negative structural change in specific brain areas.[11]

Although the human brain has a great capacity to learn new skills and become accustomed to new environments (plasticity), it has limitations in adapting in certain situations and designing paradigms to improve and sustain learned behavior. It seems that the learning tends to be specific to trained regimens but does not transfer to qualitatively similar tasks, limiting the broader utility of generic training methods.[110]

Presentations with PTSD:

The most common symptoms of PTSD include recurring unpleasant memories, frequent nightmares of the event, insomnia, loss of interest in activities enjoyed previously, feeling numb or insensitive, and unexplained or uncontrollable anger or irritability.[111-113] However, if these symptoms are unrecognized or untreated, they can progress to ominous behavioral issues, including attempted suicide.[114] Those with PTSD may present to a physician with vague constitutional symptomatology, such as chronic headaches, gastrointestinal disorders, chest pain, backaches, or feeling depressed. Treating

these symptoms alone has very little effect on the underlying PTSD or its course.[11] Humans display several defensive behaviors, depending on the proximity and severity of perceived or real threats. These behaviors include immobility/freezing, avoidance, withdrawal, aggressive defence, and complete frozen status. They may also present with defensive behavior caused by over-activation of fear mechanisms.[115] For example, PTSD and avoidance behavior may be an innate response of avoidance of, or withdrawal from perceived threats. Furthermore, heightened memory of past threats may increase avoidance of similar situations in the future. Similarly, the PTSD-associated hyper-arousal status may correspond to vigilant immobility or aggressive defence.

Assessments and the clinical diagnosis of PTSD:

Diagnostic criteria for PTSD include experiencing the original trauma through flashback of memories and nightmares and the appearance of new behavioral disorders since the incident.[26] Flashbacks or involuntary and unpleasant memories are key psychological phenomenon in which an individual has a sudden, powerful memory of a past encounter or experience.[4]

PTSD can co-exist with other common psychiatric disorders, such as mood disorder, bipolar disorder, depression, and anxiety syndromes,[30] which can cause difficulties in making the correct diagnosis and increase the likelihood of suicides.[84] Comorbidities also confuse the presentation and thus, delay the diagnosis of PTSD.[26,84] Early recognition and identification of coexistent factors would facilitate making the proper diagnoses and treatments, and thus prevent suicides. Because PTSD has an impact on an individual's psychosocial functioning and judgment; affected persons may unwittingly engage in socially unacceptable or dangerous practices.

Options of treatments for patients with PTSD:

Treatment for PTSD includes the provision of a safe, friendly, and loving environment and frequent professional counseling to evaluate and understand the current and emerging thoughts. Finding ways to help individual victims to cope with their feelings of stress, flashbacks, and other symptoms is valuable.[116] For those who have experienced significant mental trauma, part of the therapy includes facilitating learning to trust and forgive others. It is helpful to engage patients with PTSD in exercise and relaxation methods to reduce physical tension and the mental stress. In addition volunteering in local community projects is of benefit to PTSD patients. [118]

Ministries of health and defence and health departments should work closely together with all health professionals and services to provide the best possible and cost-effective services for those patients suffering from PTSD. To attain the maximum benefits, these efforts must be coordinated well. However, because of misdiagnosis or delays in diagnosis, many PTSD victims are neglected, untreated, or treated ineffectively.[11]

Role of behavioral therapy:

Cognitive behavioral programs are the main psychotherapeutic approach for treating PTSD,[119] but other approaches, including variants of cognitive or exposure therapy, have also been used.[120] The aim of cognitive behavioral therapy (CBT) is to understand how certain thoughts about the key events cause stress and PTSD, and to change the way these victims feel and react by changing the patterns of thinking, memories, and behavior.[121] CBT helps patients identify and learn the thoughts that generate fear, and substitute these with positive or less upsetting thoughts.[122,123]

CBT is an effective treatment for patients with PTSD and is considered by some psychiatric societies to be the standard of care.[115,124] Trauma-focused cognitive behavioral therapy was recommended as a first-line treatment for trauma victims, but data are not conclusive that these methods are superior to supportive and non-directive treatments.[125-128] A few reports suggest that non-allopathic approaches, such as homeopathic and hypnotic treatments, may also have a complementary role in treating psychiatry disorders in general [30] in particular, PTSD.[129,130]

Many organizations, including the United States Department of Veterans Affairs, are focusing on training both hospital and the community based mental health providers, the combination of prolonged exposure therapy [131] and cognitive processing therapy[2, 116,132] for

the care of veterans with PTSD.[1] There is also a recent initiative to reduce the stigma attached with the diagnosis of PTSD by changing its name to "posttraumatic stress injury" (PTSI) under the American Psychiatric Association DSM-5 criteria.[133]

Pharmaco-therapeutic options for PTSD:

Current pharmacologic strategies include experimental prophylactic treatments and the use of post-exposure pharmacotherapy, usually in combination with established trauma-focused psychological therapies. The non-selective beta-blocker propranalol and the selective serotonin reuptake inhibitors (SSRI) are the main groups of medications used for treating patients with PTSD. These agents decrease anxiety and stress. Efficacious interventions applied soon after trauma exposures have the potential to reduce or even prevent the development of PTSD symptoms and their associated impact on behavior and the patients' physical health. The goal of these new treatments is to modulate stress effects on memory consolidation after trauma.

Glucocorticoid, corticotrophin-releasing factor, and norepinephrine signalling modulators, as well as putative cognitive enhancers that target mechanisms of conditioned fear extinction and reconsolidation have been considered for the treatment of PTSD.[134] The latter groups of therapies include modulators of glucocorticoid receptor, glutamate signalling, positive allosteric modulators of glutamate receptors, glycine transporter inhibitors, and glycine agonists.[135] The provision of secondary pharmacologic prevention of PTSD offers an opportunity to incorporate pharmacologic and psychosocial preventative strategies.[136]

Psychological assessments and interventions should be offered to soldiers immediately after they return from deployment. Many psychiatrists also advocate group therapy as a cost-effective way of managing PTSD. However, the basis of therapy is to incorporate psychotherapy with pharmacologic agents together. Despite the wide usage, selective serotonin reuptake inhibitors as treatment of PTSD have not been fully validated.[137] Meanwhile, the value of adjunct relaxation therapies,[138,139] including meditation, as well as the re-establishment and strengthening of social supports and networks,[140] religious activities, and community support should not be overlooked as adjunct treatment modalities.[11]

Relevance of PTSD and associated disorders to society:

Post-traumatic stress disorder, depression, and psychological disorders are relatively neglected entities in most developing countries.[141,142] Consequently, inadequate resources are allocated to research and management of this disorder. Thus, there is a marked shortage of expertise and trained health professionals available to manage this condition efficiently.

Psychological responses to chronic stressful events may lead to sustained pathological stress responses.[143,144] Triggering events may be a threat of death to oneself or someone else, or threats to the physical, sexual, or psychological integrity of oneself or another that overwhelm one's ability to cope.[26] The ability of people to handle acute severe stress experiences varies tremendously among individuals. Consequently, development of PTSD may not occur in some individuals exposed to exceedingly stressful incidences, while others who have encountered seemingly less overwhelming stressors may acquire it.[5,63] Those who are psychologically prepared or trained for traumatic or dangerous experiences ahead, handle such stressful situations better [117] and thus, are less likely to experience PTSD after exposure.[84]

Outcome of treatments for PTSD sufferers:

Many diverse groups of researchers are continuing to investigate the long-term consequences of major psychological stresses; however, they are reaching conflicting conclusions.[145-149] Because of escalating wars and violence worldwide, many individuals and at times entire societies continue to experience serious traumatic events. Unfortunately, the number of people affected by war, famine, and natural disasters continues to increase, and these negative effects on people are downplayed in many developing countries.[150,151] In economically advanced countries, the majority of PTSD patients are taken care by the networks of healthcare systems and the Veteran administration in the United

States . Whereas, in other regions, including most of the Asian countries, many of the PTSD subjects are cared for by charitable organizations, friends, and family members.

The situation and the sufferings among soldiers in eastern countries during wars and post-war periods is no different from that of the soldiers returning from the battlefields of western-involved conflicts, including the Vietnam, Iraq, and Afghanistan wars.[1,106,118,142,152] In most countries, the primarily non-urban youth sacrifice their lives, limbs, eyes, and blood with the enthusiastic hope of saving their country, people, and sovereignty from internal terrorism or invading forces. However, many of them are subjected to and suffer from varying degrees of PTSD, in addition subsequently experiencing adjustment disorders. [28,39]

As with the soldiers with PTSD in the West, soldiers from other parts of the world also deserve the best possible treatment options. Because of the chronic stresses sustained due to the changes in brain chemical patterns that acquired and manifest after severe stressful experiences, the occurrence of various levels of adjustment disorders is inevitable among these groups. Thus, adjustment disorders are a part of PTSD and inseparable from it.[11] Therefore, treating them as separate entities may not have a major impact in decreasing suicidal rates or improving the situation for affected individuals.

DISCUSSION

Misdiagnosis or delays in the diagnosis of PTSD, particularly in Asian countries, have led not only to significant loss of productivity and social disruptions but also to high incidences of suicide.[23,142] The solution lies not in handling the adjustments or family issues alone, but by addressing the root causes of chronic stress, affected individuals overcome, it and improve the access and care to those with PTSD. In the long run, such solutions will improve the associated behavioral issues in a sustainable manner. With the current high suicide rates in Asian countries, it is critical to carry out an in-depth, root-cause analysis of PTSD to identify key contributory factors, warning signs, and clusters. These are culturally sensitive and thus, need to evaluate in individual society and develop practical and locally acceptable guidelines. Symptoms of PTSD are not uncommon immediately after experiencing a traumatic event. However, if they curb their normal routine and the living and working environments are not conducing, symptoms of PTSD may become chronic.[122,123]

Results from such avoid reminders of the incident, and studies in individual societies and countries should be publicized for the benefit of all countries with similar situations to focus on the real causes leading to PTSD in this group of victims. These proactive interventions would help to prevent the occurrence of PTSD and enable a knowledge-based therapeutic approach to cost-effectively treating and curing PTSD. This would benefit the military personnel as well as affected civilian victims and facilitate alleviating chronic stresses and suicides among vulnerable soldiers and officers in armed forces and the police, and the civilians. Such in-depth studies should help implementing of specific diagnostic and country-specific therapeutic guidelines to plan actions to assist soldiers and civilians before, during, and after a war situation; it would also lead to proper utilization of resources.

With the availability of extensive medical facilities in the west, including in the United States, fewer than half of those who are affected are treated for PTSD. [142,153] Healthcare workers in armed forces and the ministries of defence and its network of health professionals in any given country and the department of health and healthcare services should pay more attention to these post-war victims, both civilians and soldiers.

Labeling soldiers with PTSD as having an “adjustment disorders" is an injustice and will not help these victims.[154] This practice needs to be changed because it provides little help to these patients and their families. Meanwhile, care should be taken not to interfere with spontaneous recovery. Unless healthcare providers can actively intervene with validated therapies and provide a wider-based support to the victims and their families, the high incidence of suicide and significant behavioral

issues are likely to rise, which will lead to loss of productivity, loss of more lives and more family disruptions.

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