

Review Article

Understanding the predisposing risk factors of young suicide

Rashmi Wardhan¹, Padmshree Mudgal^{2*}

¹Department of Biochemistry, Shivaji College, University of Delhi, Delhi, India

²Department of Biochemistry, Daulat Ram College, University of Delhi, Delhi, India

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*Correspondence:

Dr. Padmshree Mudgal,

E-mail: padmshree.m@gmail.com

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ABSTRACT

Suicide is an unfortunate multifactorial problem impacting families and communities. Many young lives are lost every year due to suicide. There is an urgent need to understand the multifactorial risk factor mechanisms providing vulnerability to suicidal behavior for early detection of impending incidents, monitoring, and prevention. This review aims to give an insight into the various biochemical and genetic markers along with the associated socio-economic factors and mental disorders which contribute to increased suicide risk. The role of different neurotransmitter-associated pathways such as serotonin, gamma aminobutyric acid (GABA), and norepinephrine pathway, and pathways involving the hypothalamic-pituitary-adrenal (HPA) axis, lipid metabolism, and neuroinflammation in suicide ideation and risk have been explored. Understanding of these predisposing factors and associated pathways could help identify the risk and lead to the development of drugs/ treatment to prevent suicides.

Keywords: Suicide, Risk factors, Biochemical markers, Genetic markers, Neuroinflammation, Socio-economic factors, Mental disorders, Substance abuse

INTRODUCTION

Suicide is a very sad and unfortunate event done at a personal level which leaves never-ending pain for the family and friends and indirectly impacts society and the country as a whole. Suicide is defined technically as self-directed injurious behavior with the intention to die and resulting in death. It is different from a suicidal attempt which is a non-successful action and from suicidal behavior, which is a self-directed intention to harm oneself.¹ Suicide is the third leading cause of death in 15-19 years old. As per World Health Organization (WHO) data, 8 lakh people die due to suicide every year.² Suicide rates vary substantially between different regions of the world depending on multiple factors and one of them is financial parameter as more than 80% of all suicides occur in countries having low or middle-income.³ Suicide mortality rates vary from 15.6 per 100,000 in inhabitants of South-East Asia to 5.6 per 100,000 in the Eastern Mediterranean region. The youth, which falls in the age

group of 15-29 years, is found to be the most vulnerable group. They find themselves unable to cope up with many new challenges of life. They are at a stage of life when they have to develop their own identity, build self-esteem, acquire new skills, and gain academic excellence to build up a career, self-independence, and confidence to survive. At the same time, they are undergoing physiological and psychological changes. In today's times, the social media and the self-projection to the outside world are putting added pressures. Alcohol and substance abuse is also increasing among the youth. All these factors together impact the mental status of a young mind.⁴

Disruption of various biochemical pathways, such as serotonin, gamma aminobutyric acid (GABA), and norepinephrine pathway, responses such as stress response involving hypothalamic-pituitary-adrenal (HPA), immune response leading to neuroinflammation, and change in molecular homeostasis can lead to increased vulnerability to suicide.⁵ Other factors such as socio-

economic, mental disorders such as depression, schizophrenia, and bipolar disorder, and substance abuse also contribute to increased risk.

Recently a global pandemic caused by a coronavirus disease 2019 (COVID-19), infected more than 36 million people and had a profound impact on the psychological and social wellbeing of people of all age groups.⁶ Long periods of lockdowns, social isolation, fear of getting infected, especially among health workers, loss of income, and jobs have led to increased anxiety, fear, and depression contributing to increased suicide rate during the pandemic, especially in youth.⁷ While some people overcome and pass through the traumatic experiences of their life, some succumb to it and take drastic steps like suicide. The psychological, genetic, epigenetic, and physiological factors might play an important role in the individual decision, which might impart susceptibility in suicide or suicidal behavior. There are several reports about increasing numbers of depression, suicidal behavior, suicidal attempts in society, but people shy to address and recognize this as a disease because of social stigma and ignorance. Hence it becomes very pertinent to look into the risk factors contributing to increased suicide rate amongst the youth and look for solutions to prevent it. In this review article, the authors have summarized the role of various biochemical pathways and molecules which are involved in brain signaling and are required for good mental health. Dysregulation of these biochemical markers increases the vulnerability of youth to succumb to various stress parameters.

SUICIDE RISK FACTORS

Biochemical markers

As young lives are lost prematurely to suicides, understanding the neurobiological mechanisms of suicidal behavior becomes even more relevant to predict suicide risk and prevent it.⁸ The biochemical pathways which have been studied and have yielded valuable information involve the neurotransmitter systems, HPA axis, neuroinflammatory indices, neurotrophic factors, and lipoproteins.⁹

Serotonin system

The role of the serotonin signaling pathway has been known to be implicated in suicide. Low levels of 5-hydroxy indole acetic acid (5-HIAA), the main metabolite of serotonin (5-hydroxytryptamine, 5-HT) in the cerebrospinal fluid (CSF) has shown a positive correlation with suicide and is a proposed biochemical marker for suicide.¹⁰ Post-mortem autoradiography studies in suicide cases of the serotonin transporter (SERT) and the 5-HT_{1A} and 5-HT_{2A} receptor have found that a decrease in transporter binding and an increase in 5-HT_{1A} and 5-HT_{2A} binding is confined to the anterior cingulate cortex, hypothalamus, occipital cortex, brainstem, and ventral prefrontal cortex (PFC).¹¹ An increase in 5-HT_{1A} and 5-

HT_{2A} receptors in PFC suggests inhibition of excitatory output from cortical regions that mediate executive function and behavioral restraint. It is hypothesized that reduced cortical activity may be a top-down cause of a reduction in restraint and an increase in the risk for suicidal behavior. The serotonin transporters (SERT) which are present on axons and axon terminals are indicative of serotonergic innervation and intrasynaptic serotonin levels.¹² Low SERT expression on axonal membranes in depressed and suicide victims suggests the greater SERT internalization secondary to less intra-synaptic 5-HT. Up regulation of postsynaptic 5-HT_{1A} and 5-HT_{2A} receptors in the prefrontal cortex, reduction in serotonin transporters in the prefrontal cortex, hypothalamus, occipital cortex, and brainstem is observed in the postmortem of suicide cases. 5-HT_{1A} up regulation is observed in the ventral prefrontal cortex, a region that is involved in behavioral and cognitive inhibition.

GABA

GABA is the major inhibitory neurotransmitter in the brain which acts as the "brakes" for neural activity and its dysfunction is implicated in a wide range of neuropsychiatric disorders. GABA neurons expressing somatostatin (SST), neuropeptide Y (NPY), and cortistatin (CORT) target and inhibit the dendrites of pyramidal neurons, whereas interneurons expressing parvalbumin and cholecystokinin target the cell body and axon initial segment. GABA plays an important role in the down regulation of the HPA-axis in response to acute stress. GABA acts by binding to GABA-A receptors in CRH neurons in the hypothalamus including the PVN.¹³ GABA acts via two receptors: GABA-A (a postsynaptic, ligand-gated chloride channel) and GABA-B (a presynaptic receptor which modulates neurotransmitter release). The observed alteration of GABA function in major depression is linked to altered GABA-A receptor function. Increased methylation in the GABA-A receptor promoter is suggested as a potential molecular mechanism for the downregulated expression in suicide victims.¹⁴

A recent study reported that the GABRA6 gene (encodes the GABA-A receptor alpha-6 subunit) variant plays an important role in mediating the stress-induced suicidal risk-related phenotypes. Specifically, GABRA6 T carriers showed an increased suicide risk after exposure to stressful life events.¹⁵

Norepinephrine

Norepinephrine (NE) is one of the most studied catecholamine neurotransmitter in the brain in relation to suicide risk as well as psychiatric disorders. NE is secreted majorly by neurons in the locus coeruleus (LC), which is located at the pontomesencephalic junction at the floor of the fourth ventricle in the pontine region of the brain.¹⁶ The NE containing fibers emanating from the LC then innervates the entire brain. The rate-limiting step in NE biosynthetic pathway from the amino acid tyrosine is

hydroxylation of tyrosine by tyrosine hydroxylase. NE biosynthesis is regulated by changes in phosphorylation-dependent tyrosine hydroxylase activity or by changes in the expression of the tyrosine hydroxylase gene. The NE in brain noradrenergic neurons is then packaged into vesicles via the vesicular monoamine transporters (VMAT2) and released into the synaptic cleft via calcium-dependent exocytosis. NE mediates its effect through either $\alpha 1$ (A, B, D)-, $\alpha 2$ (A, B, C)-, $\beta 1$ -, or $\beta 2$ -adrenoceptors. NE release is additionally regulated by adrenoceptors, while activation of presynaptic $\alpha 2$ -adrenoceptors (autoreceptors) inhibits NE release, activation of presynaptic $\beta 2$ -adrenoceptors stimulates NE release. The action of NE at the synaptic cleft is terminated largely through the reuptake of the neurotransmitter by the NE transporter. NE is then degraded by monoamine oxidase (MAO).¹⁷

Suicidal and depressed patients have a decreased number of NE neurons in the locus coeruleus.¹⁸ Depression is characterized by 'noradrenergic deficiency syndrome'. A new line of treatment of depression which often leads to suicide is noradrenaline reuptake inhibitors.¹⁹ Stress-activated neurotransmitters such as glutamate and GABA, and stress hormones such as CRF and cortisol, have profound effects on noradrenergic neuronal activity. Glial dysfunction may also be contributing to monoamine deficiency.

Stress pathway

The HPA axis is a network that connects the hypothalamus, pituitary gland, and adrenal glands and is involved in stress response. In response to stress, the HPA axis is stimulated and corticotrophin-releasing hormone (CRH) is released from the hypothalamus, which then activates the corticotrophs in the pituitary gland to secrete adrenocorticotrophic hormone (ACTH). The ACTH then stimulates the adrenal glands to synthesize and release the stress hormone cortisol. Under chronic stress, blood cortisol levels are much increased. Mood disorders and suicidal behavior has been associated with dysregulation of the HPA axis in response to stress. Hypothalamic activation of the HPA axis is modulated by several neurotransmitters, both inhibitory (GABA and opioids) and excitatory (norepinephrine and serotonin) on the periventricular nucleus (PVN). The secretion of CRF and ACTH are controlled by sensitive negative feedback exerted by cortisol by binding to its receptors in the pituitary and hypothalamus.²⁰ Studies on haplotypes of the FKBP5 gene which expresses protein 5 modulates cortisol receptor activity and is strongly associated with suicide.²¹ The dexamethasone suppression test (DST), which tests the feedback regulation showed dysregulation of the HPA axis in participants with suicidal behaviors, and the Trier social stress test (TSST) which tests the stress response in participants showed that patients who had attempted suicide displayed a lower total cortisol output in response to stress.²² As noradrenergic over activity is associated

with the activation of the HPA axis it further heightens the suicide risk.

Lipids

Lipids as a biomarker risk factor for suicide has garnered much interest in recent times. Many epidemiologic and clinical studies have correlated the effects of lipids on mood and suicide. Major categories of lipids that have been reported to be associated with suicide risk include sterols and polyunsaturated fatty acids (PUFAs).²³

Cholesterol is an important component of cell membranes.²⁴ It plays an important role in the regulation of membrane fluidity, membrane-bound proteins, ion channels, and synaptic transmission in neuronal membranes. It is functionally required for synapse formation, dendrite formation, and axonal guidance. Cholesterol is also an allosteric regulator of neurotransmitter receptors and G protein-coupled receptors (GPCRs) in neuronal membranes. Hence, cholesterol plays a crucial role in the second messenger systems of the brain affecting the mechanism of action of antidepressant drugs and mood stabilizers. Many studies have consistently correlated low total serum cholesterol with suicide, violence, and depression.²⁵ Low total cholesterol (TC), low-density lipoprotein (LDL) cholesterol, and high-density cholesterol (HDL) cholesterol are significantly associated with higher suicide risk. Studies have shown that lower cholesterol levels over a long period of time are associated with many suicide attempts. Changes in membrane fluidity/micro viscosity due to low cholesterol concentration in neural membranes affect the function of serotonin receptors and transporters on the membrane surface. 5HT-1A receptor is the most impacted receptor in the CNS by low cholesterol levels. While cardiologists have been propagating to lower serum cholesterol and drug companies keep coming up with new cholesterol-lowering drugs, the importance of cholesterol in maintaining good mental health cannot be overlooked.

The various studies suggest a higher intake of n-3 in comparison to n-6 PUFA have beneficial effects on depression and suicide risk. Low PUFAs levels can be considered a risk factor for suicidal behavior. Low n-3 PUFA levels are also associated with the pathogenesis of major depressive disorder (MPD), bipolar disorder, and schizophrenia. FAs, cholesterol, and estrogen can interact to influence the structure and function of membrane micro domains ("lipid rafts"), with potential regulatory effects on inflammation and signal transduction, including monoaminergic signaling.²⁶

While the n-3 PUFAs have anti-inflammatory effects, the n-6 PUFAs are mainly pro-inflammatory. Elevation of the n-6 to n-3 PUFA ratio thus causes a shift toward a pro-inflammatory state. Low n-3 PUFAs activate nuclear factor kappa-light-chain-enhancer of activated B cells (NF κ B) and peroxisome proliferator-activated receptors

(PPARs). Neuro-inflammation and abnormal monoaminergic neurotransmission are the two leading biological pathways contributing to suicide.

Membrane lipid rafts regulate monoaminergic transporters and receptors in neuronal membranes. PUFA balance and cholesterol modulate the stability of membrane rafts. The lipid raft modulation has the greatest impact on suicide risk via effects on serotonin (5-hydroxytryptamine, 5-HT) transporters (SERT) and receptors. Administration of n-3 PUFA supplements is recommended to cardiac patients who are on low cholesterol intake to prevent psychiatric vulnerabilities.²⁷

Neuroinflammation

The disturbance in inflammatory cytokines has been associated with schizophrenia, bipolar disorder, and major depressive disorder for a long time.²⁸ During neuroinflammation, cytokines are secreted by peripheral immune cells, microglia, astrocytes, and neurons in the CNS. Neuroinflammation can trigger the release of pro-inflammatory cytokines such as interleukins (IL-1 β , IL-2, IL-4, IL-6, and IL-13), CRP, tumor necrosis factor- α (TNF- α), and interferon- γ (IFN- γ).²⁹ Inflammatory cytokines are also reported to be secreted in response to various simulators like vitamin D deficiency, stress, brain injury, an autoimmune disorder like multiple sclerosis, Systemic lupus erythematosus (SLE), or due to metabolic disturbances. In the brain, cytokine up-regulation is done through Toll-like receptors (TLRs) activation. Toll-like receptors are responsible for innate immune response during infection. Among all the TLRs expressed in humans, TLR3 and TLR4 appear to be unique and important in brain function. TLR-4 activates an intracellular cascade that ultimately causes translocation of NF κ B to the nucleus where it initiates transcription of cytokines that are both pro- (interleukin (IL)-1 β , IL-6 and TNF α) and anti- (IL-1 receptor antagonist (ra), IL-10) inflammatory in nature. Studies by Pandey et al showed that the mRNA and protein expression of TLR3 and TLR4 was significantly increased in the dorsolateral prefrontal cortex (DLPFC) of depressed suicide victims as compared to control.³⁰

The inflammatory cytokines enhance suicidal behavior by activating the kynurenine pathway of essential amino acid tryptophan catabolism, dysregulation of the HPA axis, and alterations in monoamine metabolism. Indoleamine 2,3-dioxygenase (IDO) or tryptophan 2,3-dioxygenase (TDO) catalyzes the first step of tryptophan catabolism to form kynurenine, which is further converted into quinolinic acid (QUIN) and kynurenic acid (KYNA). Inflammatory cytokines like IFN- γ , IL-6, IL-1 β , and TNF- α positively modulates IDO and/or TDO activity.³¹

A study by Erhardt et al reported that the QUIN levels in CSF of suicide attempters showed a 300% increase as compared to the levels in healthy controls. The CSF QUIN levels were found to be highest at the time of a suicide

attempt, but the levels remain significantly elevated over a period of 2 years. In the brain, QUIN is primarily produced by microglial cells and infiltrating macrophages. One of the mechanisms associated with its neurotoxic effects is via the activation of the glutamate N-methyl-D-aspartic acid receptors (NMDARs). QUIN also increases glutamate release by neurons and inhibition of its uptake and degradation by astrocytes. This results in elevated extracellular glutamate levels and stimulation of the glutamatergic system. Hyper stimulation of NMDAR by QUIN could be a major contributing factor to the pathophysiology of depression and suicidal behavior.³²

Kynurenic acid (KYNA) is a glutamate receptor antagonist shown to inhibit a range of ionotropic excitatory amino acid receptors, including NMDARs, AMPA receptors (AMPA), and kainate receptors. Additionally, KYNA inhibits α 7 nicotinic acetylcholine receptor (α 7nAChR) and interacts with the aryl hydrocarbon receptor and an orphan G protein-coupled receptor GPR35.³³ Activation of GPR35 brings about a reduction of extracellular brain glutamate levels and prevents the release of pro-inflammatory cytokines. Hence, KYNA and QUIN have opposing effects on the NMDAR. The levels of KYNA are significantly decreased in patients with severe depressive and suicidal symptoms.³⁴ The CSF QUIN/KYNA ratio has been reported to be more than 2-fold elevated in suicide attempters compared to healthy subjects, suggesting a direct correlation between an increase in NMDAR and suicidal tendencies.

Genetic markers

Search is on to find the link between suicidal behavior and specific genes. It has been known that suicidal tendencies run in families. Most of the early molecular genetics studies to determine that heritable factor focused on the serotonin pathway. Bondy et al identified two genes, one coding for the tryptophan hydroxylase 1 (TPH1) and the other, the serotonin transporter (5-HTTLPR), which showed significant involvement in the vulnerability for suicidal behavior.³⁵ Tryptophan hydroxylase (TPH) is the rate-limiting enzyme in the biosynthesis of 5-HT, converting the amino-acid tryptophan to 5-hydroxytryptophan (5-HTP) which is further decarboxylated into 5-HT. Two isoforms of TPH, TPH1, and TPH2 have been identified, both being located on different chromosomes, chromosomes 11 and 12, respectively. The intronic polymorphisms (A218C and/or A779C) of the tryptophan hydroxylase 1 (TPH1) gene, is found to be a quantitative risk factor for suicidal behavior. The S-allele of the serotonin transporter polymorphism (5-HTTLPR) has shown to be associated with aggressive violent behavior and not directly linked with suicidal attempts. Similarly, single nucleotide polymorphisms (SNPs) of the MAO may not have a direct relation to suicidal behavior but may increase suicide risk via violent act.³⁶ MAO A and B gene are associated with impulsive-aggressive personality traits.

A significant increase in catecholamine-O-methyltransferase (COMT) (the enzyme that transfers a methyl group from S-adenosyl methionine (SAM) to catecholamines) mRNA in the brain cortex was reported in depressed and suicidal cases.³⁷ The SNP rs4680 (code methionine (Met) in place of valine (Val) at 158 position) in gene reduces one-fourth of enzyme activity in the dorsolateral PFC. The persons with methionine polymorphism instead of valine are more prone to depression in adverse life incidents like physical abuse, malnutrition, or drug abuse in contrast to the valine allele.³⁸ SNP rs4680 polymorphism in the COMT enzyme gene is associated with predicted lower dopamine synthesis in the midbrain which may affect connectivity with the PFC and higher suicide risk. Single nucleotide polymorphism may affect males and females differently as seen in the Swedish population, where the Met/Met or Met/valine genotype has shown a higher risk of depression in males than women.

Mental disorders

There is a strong association of suicides with mental disorders, depression, and psychosis.³⁹ 90% of the people who commit suicide are suffering from one or more psychiatric disorders. Patients with bipolar disorder are reported to be at the highest suicide risk (odds ratio (OR)=7.77) than unipolar affective disorder (OR=6.67), followed by schizophrenia (OR=6.55) and anxiety disorders (OR=3.57-6.64).⁴⁰

There is a relation between cognitive function and suicidality in depressive patients. The depressed patients with suicidal ideation show cognitive alterations in attention and psychomotor speed and executive dysfunctions (low performance in executive function (EF) test). Dysfunction in EF would impact reasoning, problem-solving, planning, decision making, and positive thinking, among other behaviors. These cognitive alterations and impulsive behavior are strongly linked to suicidality. Such patients present self-injuring behavior, including suicide and suicide attempts, especially when confronted with stressful situations.⁴¹ Dysfunctional EF could become an identifiable endophenotype or “marker” in clinical studies linking suicidal tendencies in depressive patients.

The risk of suicide death in BD is up to 10-30 times higher than that of the general population.⁴² BD is marked by severe mood swings. Patients experience high-energy, elevated moods during manic episodes and sad, hopeless, and despair during depressive ones. People with bipolar also experience psychotic symptoms such as hearing voices or having delusions or hallucinations. Such patients also experience social exclusion, stigma, and discrimination that further increases suicide risk.⁴³

40% to 50% of schizophrenia patients report suicidal ideation at some point in their lives. Such patients may experience several psychotic symptoms such as suspiciousness, paranoid delusions, mental disintegration

and agitation, negative symptoms, depression and hopelessness, and command hallucinations (such as voices commanding them to kill themselves). Recent studies show that prefrontal cortex-based circuit dysfunction may contribute to suicidal thoughts in the early stage of schizophrenia.⁴⁴

Traumatic experiences such as adverse childhood experiences (ACE) due to physical or sexual abuse, loss of a parent, or conflict at home can trigger lots of emotional responses, which can result in post-traumatic stress disorder (PTSD), depression resulting in an increased risk of suicidal behavior.⁴⁵

Substance abuse

Substance use is a high-risk factor for suicide ideation and attempts in both fatal and nonfatal doses. Individuals with alcohol dependence and persons who take drugs have a 10-14 times greater risk of death by suicide as compared to people who have no dependence.⁴⁶ Substance abuse may impair judgment, weaken impulse control, and disrupt neurotransmitter signaling pathways, leading to higher suicidal tendencies. Drugs can perturb synaptic transmission in the brain, which can result in acute behavioral effects such as, euphoria, sedation, or stimulation. Addiction to drugs can lead to the disruption of neural circuits in the brain.

The risks increase many folds if substance abuse is associated with comorbidity of depression (MDP) or other mental health disorders such as PTSD, anxiety, BD, schizophrenia, and some personality disorders. People who suffer from depression or other mental disorders often turn to drugs or alcohol as a coping mechanism. Many studies have shown that oxidative stress (OS) plays a critical role in the manifestation of behavioral impairments observed in patients with alcohol abuse.⁴⁷ The cytochrome P450 enzymes (CYP2E1) that are involved in ethanol metabolism in the liver, as ethanol is oxidized to acetaldehyde. The CYP2E1 generates reactive oxygen species (ROS) and exposure to ethanol therefore results in the accumulation of ROS and nitric oxide. Increased ROS induces oxidative stress that affects the neuronal cell in the brain, resulting in neurotoxicity or neurodegeneration.⁴⁸

Socio-economic factors

In India, the official suicide rate for 2015 published by the National crime records bureau (NCRB) of India was 10.6 per 100 000 population, almost the same as the global average of 11.4 per 100 000 population.⁴⁹ As suicide attempt is a punishable offense under the Indian penal code (IPC Section 309); these figures may be much higher as many cases may go unreported, unlike western countries. The data in India might be misleading sometimes. There are many socio-economic factors known for increasing suicide risk. More research, meta-analysis, and data mining may provide a better and clear picture for the

planning and implementation of effective suicide prevention programs.⁵⁰

Gender

The Indian NCRB data over the period from 2004 to 2013 show that the maximum suicide deaths have occurred in 15-29 years age group for women and 30-44 years age group for men. The overall male: female (M: F) ratio of suicide victims over the 10 years has shown an increase from 1.8 to 2.1. This is much lower than European countries and the United States, where the male suicides far outnumber female suicides (M:F = 3:1-4:1). The higher rates of female suicide in Asian countries is linked to the position of women in the traditionally patriarchal societies of Asia. Exploitation, low self-esteem, and self-worth, economic dependence on males, physical and sexual abuse, family and social pressures, and social inequality are some of the factors which impact women's mental health in these patriarchal societies.⁵¹

Occupation

High suicide risk is associated with many occupations such as farmers, doctors, nurses, dentists, veterinarians, pharmacists, the police, the military, and sailors, and artists. A major determinant of high suicide rates in most of these occupations is the ease of accessing the means to commit suicide (medicines, chemicals, guns, or drowning). Studies suggest that stress and access to lethal compounds contribute to suicide. The lower-skill occupations are found to be at a greater risk than the ones with higher skills. Job insecurity, long working hours, work-home imbalance, and high-risk stressful jobs contribute to increased mental stress. In India, approximately 16,000 farmers die by suicide each year because of low income and large debts. The lowest rate of suicides has been observed in teachers, educators, and librarians. The reason may be their job security and professional satisfaction. High stress, low income, poor job satisfaction, and poor education as major risk factors.⁵²

Academic stress

In 2019, at least one student died by suicide every hour in India. According to the NCRB, 10,335 student suicides were reported in 2019.⁵³ The latest data released by the NCRB reported that more than 90,000 young adults died by suicide in 2019 in India. Behavioral problems and suicides are on a rise amongst the young, 12 percent of Indian students between the age of 4 and 16 suffer from psychiatric disorders, and 20 percent show signs of mental disorders.⁵⁴ Examination related causes are becoming one of the major causes of student suicides. Marks based education system deciding on the academic future of a student puts enormous pressure and stress on the child added to that are pressures of parents and peers to perform well. Academic pressures leave very little time for healthy activities like sports, exercise, or even human interaction. The inability to cope with pressures, high expectations,

less human interaction and activities are driving more and more youth towards despair, depression, and suicides.

CONCLUSION

The biochemical and genetic markers could develop as important parameters to recognize the vulnerability of an individual to suicide risk. The nutrition and physical health contribute at the molecular level in the regulation and secretion of neurotransmitters affecting behavior in various age and sex groups. Socioeconomic, education, and stress affect indirectly the secretion of brain signaling molecules and hormones to impact behavior. In this paper, the authors have explained the role of the various biochemical pathways and susceptible genes which may contribute to the vulnerability of youth to suicidal behavior. These pathways can be modified and differently regulated to increase resistance at the cellular level and prevent suicide ideation and risk. More extensive research is required to establish a direct link to suicide and suicidal behavior to recognize and monitor the vulnerable population. Early detection of identified markers, education of health workers, family members, and concerned individuals would have a positive impact in preventing suicides.

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