**Running head:** *Serum lipids and neurobiology of suicide*

REVIEW ARTICLE

**Neurobiology of impulsivity and aggression as substrates of suicidal behavior: A narrative focus on the involvement of serum lipids**

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**Abstract**

Previous incidental findings of an increase of suicidal risk among subjects with low cholesterol levels have drawn attention to the role of lipids in suicidal behavior. To date, multiple lines of evidence acquired from clinical studies have confirmed an association between low cholesterol levels and suicidal behavior, but the involvement of dimensional traits including impulsivity and aggression in this association remains elusive. In this narrative review, we aimed to address and synthesize the literature regarding the involvement of lipids in the neurobiology of suicidal behavior and its underlying psychological substrates, impulsivity and aggression. An electronic database search was performed using different combinations of relevant keywords. Both preclinical and clinical studies matching the scope of this article were reviewed and filtered through an inspection of the abstracts to recruit the most suitable articles that contributed essential and substantial findings to the literature. Although subject characteristics and study designs vary across studies, current research has demonstrated that impulsivity and aggression might have shared neurobiologic substrates involved in altered serotonergic neurotransmission. Despite the association between low serum lipid levels and suicidal behavior being well documented, the involvement of lipid subtypes in the pathophysiology of impulsive and aggressive traits remains elusive. Further work is warranted to recognize the roles of lipids in neuronal membrane functions and serotonin metabolism, promote a greater appreciation of identifying biomarkers that could be used to determine at-risk individuals, and develop potential interventions to disrupt the pathogenesis of behavioral phenotypes of suicide.

**Keywords:** aggression; cholesterol; impulsivity; lipids; neurobiology; suicide; suicidal behavior

"*But in the end one needs more courage to live than to kill himself.*"

Albert Camus, 1971

## Introduction

Suicidal behavior is a major cause of mortality and morbidity worldwide. It has been estimated that approximately 800,000 people die by suicide each year, and the number of non-fatal suicide attempts is 10-20 times more frequent, indicating that suicidal behavior needs to be addressed as a real public health priority (1,2). To date, numerous neurobiologic models have been postulated to elucidate the etiology of suicidal behavior, and the stress-diathesis explanatory model has been developed to reveal the complex interplay between neurobiologic factors that possess a susceptibility to suicide such as genetic risk variables, altered serotonergic function, and psychosocial stress responses potentially leading to suicidal behaviors (1,3). This model suggests that vulnerable individuals give abnormal or exaggerated responses to otherwise neutral stimuli (4). Furthermore, advanced neuroimaging techniques have enabled researchers to examine this model regarding the association between brain regions and neurochemistry in emotional, cognitive, and behavioral components of suicide (5).

Over the last decades, attention has been drawn to the fact that people who commit suicide have a certain predisposition (6,7), which appears to be mediated and moderated by a number of individual differences in personality, particularly impulsive and aggressive traits (8,9). There is a considerable line of evidence that suicide attempters and completers have higher levels of impulsivity and aggression (10), independent of the psychopathology (9). Evaluation of impulsivity and aggression is pivotal in suicide research and of clinical importance because both are cardinal dimensions of many psychiatric entities, including personality disorders (11). Although impulsivity and aggression share a considerable amount of common psychobiological substrates, there are many complex interactions between genes, biologic signaling, neural circuits, and the environment, all of which are involved in the development and expression of aggression and impulsivity. Aggression is classified in two forms; reactive/impulsive and proactive/premediated (12). Despite suicidal behavior having premediated or proactive characteristics to an extent, many authors have considered suicidal behavior as an impulsive self-

aggressive behavior (13); therefore, research into suicide has focused on the common neurobiologic substrates of impulsivity and aggression. To date, the neurobiologic and genetic research of impulsivity and aggression has largely focused on the dysfunction of the serotonergic system (14). A central hyposerotonergic neurotransmission has consistently been suggested to be associated with impulsive aggression and suicidal behavior (15). On the other hand, neurobiologic substrates that result in impaired serotonergic function tend to be influenced by environmental factors such as childhood traumas and stress, and many psychiatric disorders that are recognized to be triggered by environmental stressors have been associated with decreased serotonergic neurotransmission (16).

There are several lines of evidence showing the involvement of cholesterol and other lipids in synaptic plasticity, neuronal functioning, and behavior (17,18). Serum lipids have also received attention as potentially meaningful biomarkers for suicidal behavior recent years. Such interest has been inspired by prior studies that linked serum lipid alterations and major depressive disorder (MDD) (19). Despite the association between low serum cholesterol and both impulsivity and aggression being documented previously (20,21), the association with serum lipids among suicidal populations has received less attention in related studies. In this review, we aimed to address the involvement of serum lipids in the impulsivity and aggression dimensions of suicidal behavior, and synthesize the literature regarding possible neurobiologic explanations that may reveal the effect of lipids on the neurochemical substrates of suicide and its behavioral dimensions.

**Box 1 to be inserted here**

**Neurobiologic underpinnings of the association between lipids and impulsivity as a substrate of suicidal behavior**

Impulsivity, a common substrate of suicidal behavior (22-25), is a complex and multidimensional construct in most theories of personality, and conceptualized as swift action without forethought or conscious judgement, behavior without adequate thought, and the tendency to act with less forethought than do most individuals of equal ability and knowledge (26). Impulsive behaviors encompass a broad range of behaviors that reflect impaired self-regulation, such as poor planning,

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responding prematurely before considering consequences, risk-taking, sensation-seeking, and an inability to inhibit responses and preference for immediate over delayed rewards (27). Developmental psychopathology theories approach impulsivity as an amplification of a normal trait that shows a range of individual differences in normal populations (28). Impulsive behavior may be driven by genetic and temperamental characteristics, and pharmacologic and neurobiologic factors that interplay with psychological and environmental experiences unique to the individual (25,29-31).

The neurobiology of impulsivity can be conceptualized as an imbalance between the top-down control provided by the limbic structures of the prefrontal cortex (PFC) including the orbital frontal cortex (OFC) and the anterior cingulate cortex (ACC), and the bottom-up drives generated in the limbic structures such as the amygdala and insula (32,33). In fact, despite there being well-documented neuroanatomic changes related to impulsivity, alterations in the activity and functions of corticolimbic and corticostriatal circuits without overt neuroanatomic changes have more pronounced involvement in the cognitive, emotional and behavioral basis of impulsivity (5). Serotonergic neurotransmission has a cardinal role within these circuitries and serotonin regulates the prefrontal and limbic functions by acting on $5-HT_2$ receptors (25,34,35). The most consistent finding regarding the relationship between impulsivity and serotonergic functions is that the reduced central serotonergic neurotransmission is associated with increased levels of impulsivity (33,36,37). Although conflicting results have been reported at the receptor level, it has been suggested that agonism of $5-HT_{2A}$ and antagonism of $5-HT_{2C}$ in frontolimbic structures are associated with the increased levels of impulsivity (12,32).

The complex relationship between serotonergic activity and impulsivity has attracted interest to conditions that alter both serotonin release and receptor functions. One such condition might be alterations in lipid metabolism (38). Both preclinical and clinical studies that examined the association between lipids and impulsivity primarily attempted to reveal the interplay between changes of cholesterol and central serotonergic neurotransmission, which has been found in the emergence of impulsive behavior. Kaplan et al. demonstrated that low levels of serum lipids in macaques exposed to cholesterol-restricted diet exhibited more impulsive aggressive behaviors compared with counterparts on a normal diet (39). The authors postulated a cholesterol–serotonin hypothesis of aggression, which

suggested that low levels of cholesterol led to impulsive behaviors through altered serotonergic functioning.  In a recent rodent model, Vevera et al. administered simvastatin, a hydroxymethylglutaryl coenzyme A (HMG-CoA) reductase inhibitor that lowers serum cholesterol, to rats for four weeks. They demonstrated that in medicated subjects, which had exhibited behavioral changes including impulsive behaviors (40), the reduction of cholesterol levels in the brain tissue was associated with decreased serotonin uptake into platelets and decreased membrane microviscosity as measured in erythrocytes (41). The behavioral measurement method that they used was prototypic in the plus-maze test, examining anxiety and impulsivity-driven behavior, and their findings were congruent with the notion that a reduction of central serotonergic activity led to a greater number of entries of the subjects into the open arms of the plus-maze, indicating increased anxiety and impulsivity (42).

Another postulation establishes an association between either low or high peripheral and cholesterol levels and serotonergic hypofunction, based on cumulative evidence that cholesterol influences the conformation and the function of membrane-bound receptors by reducing neuronal membrane fluidity and increasing the mechanical strength of the membranes (43). Becher et al. asserted that specialized microdomains, called lipid rafts, which exist within plasma membranes, were involved in the satiety and stability of neuronal membranes, while serving as assembly platforms for signaling complexes (44), and altered cholesterol levels in extracellular microenvironment led to a disrupted constitution of cellular membranes, which might be associated with a disruption of the normal function of lipid rafts (43). In particular, lipid rafts have been shown to regulate γ-aminobutyric acid receptor B (GABA_B receptors) activity, and an impairment in GABA_B receptor signaling due to disarrayed lipid rafts may lead to disrupted serotonin release (45). Cholesterol may also affect serotonergic function indirectly by binding itself tightly to transmembrane ion channels, enzymes, and receptors (46). Clinical studies among patients with hypercholesterolemia have shown lower serotonergic activity through blunted serotonin-mediated vasodilation in forearm arteries and lower platelet serotonin concentrations compared with healthy controls (47,48).

Both preclinical and clinical studies suggested that either high or low levels of cholesterol might result in serotonergic dysfunction through different mechanisms. Tomson et al. examined the effect of

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serotonin 5-HT$_{2A}$ receptor gene polymorphisms on impulsivity and whether serum cholesterol moderated such an effect in a cohort comprising healthy young adults (49). They reported that cholesterol levels had no main effect on impulsivity measures but rather had complex interaction effects with the HTR$_{2A}$ genotype and sex, and high total and low-density lipoprotein (LDL) cholesterol levels moderated the effect of the HTR$_{2A}$ gene promoter polymorphism. This study also highlighted the importance of sex in the analysis of gene and behavioral interactions; in female subjects, high LDL and total cholesterol levels increased the genotype effect. Another study conducted by Troisi showed a weak correlation between total cholesterol (in a range of 110-295 mg/dL) and impulsivity among patients with mood disorders (20).

Such variability between the findings of studies regarding the relationship between cholesterol, serotonin, and impulsivity may be related to the notion that serotonin neurotransmission is not the sole neurochemistrical process involved in the occurrence of impulsive behaviors; dopamine, noradrenaline, glutamate, and GABA may also be involved in the multifaceted balance between top-down control and bottom-up drives of stimuli, which are regulated by frontolimbic circuitries (32,50). Any deficiency in frontolimbic circuitries, serotonergic or not, may lead to an increase in the response to salient or neutral stimuli an consequent impulsive behaviors. Clearly, there is a lack of consistent findings regarding the relationship between lipids and the serotonergic system in the context of impulsivity. A transdiagnostic approach is needed to examine the relationship between trait impulsivity and cholesterol levels, which may be moderated by serotonergic neurotransmission, among larger samples.

**Neurobiological and lipidergic correlates of other-directed and self-directed aggressive behavior**

Aggression refers to a wide, complex, and heterogeneous spectrum that includes emotional, cognitive, and behavioral dimensions (51), and is usually interchangeable with aggressive behavior, which is any physical or verbal action intended to harm another person who is motivated to avoid being harmed (52). Aggressive behavior is often distinguished from a high level of trait aggression, the latter identifying people who are prone to engaging in physical and verbal aggression (53). Aggressive behavior is often engendered by actions or situations that are aversive or stressful (33,54,55).

Aggression, which is recognized to be functional in order to survive to some extent, and is inherent among the behavioral repertoire of all living organisms, has many negative outcomes and is associated with many clinical adversities including suicidal behavior. Multiple lines of evidence obtained from epidemiologic, clinical, retrospective, prospective, and family studies have identified a strong link between aggression and suicide (10,56-58). It has been found that many individuals who attempted suicide had significantly higher scores in lifetime and trait aggression (58-61). Thus, much of the work on the interrelationship of suicide and aggression has focused on personality traits and psychiatric diagnoses related to self-reported hostility and aggression (60). Despite impulsive or reactive nature of aggression being commonly attributed to the emergence of suicide, suicidal behavior including suicidal ideation has been suggested to involve both reactive and proactive types of aggression (13,62). A growing body of evidence suggests common neurobiologic substrates of suicide and other forms of aggressive behavior (3,63).

The association between violent and aggressive behavior and low serum cholesterol levels has been consistently confirmed by extended research (64). Meta-analyses of cholesterol-lowering trials have shown that more violent deaths by suicide were found among patients whose cholesterol had been reduced (65). An association between low cholesterol levels and violent behavior has also been found in individuals with a history of criminality, anti-social personality disorder, and conduct disorder, who had not undergone any cholesterol-lowering interventions (66-68). In addition, low serum cholesterol levels were found in groups of patients that exhibited self-directed aggression including self-mutilation. (69-73).

Psychological correlates of aggression including emotion, motivation, cognitive functions, and behavior are driven and nourished by extensive neural pathways and neuroendocrine mechanisms (74). Similar to impulsivity, serotonergic neurotransmission is the most-studied neural function in the physiology of aggression (74). In recent decades, it has been shown that there is an inverse relationship between serotonin concentrations in the synaptic cleft in the brain and the expression of aggressive behavior (75). Such a relationship was demonstrated in the early work of Kaplan et al., who artificially manipulated the amounts of cholesterol consumed by cynomolgus macaques, and animals who were fed

with a low-cholesterol diet were found to have significantly lower serum cholesterol levels, be more aggressive, and less affiliative (39). Their findings indicated that the a low-cholesterol diet simultaneously affected serum cholesterol levels, which might directly influence the neural pathways of behavior through altered serotonergic activity. Buydens et al. demonstrated simultaneous associations between low HDL cholesterol and indices of altered serotonergic function, which supports previous findings (64).

Despite the exact mechanisms underlying the association between lipid profile and aggressive behavior having no yet been elucidated, it has been suggested that reduced serum cholesterol could decrease the cholesterol/phospholipid ratio in neuronal membranes with consequent alterations in membrane fluidity, viscosity, and function, leading to alterations in the function of 5-HT receptors and of the 5-HT transporter (76,77). Numerous studies indicated that changes in serum cholesterol via lipid-lowering medication affected the structure of neurons and cellular neurochemical processes, including serotonin receptor activity, which might lead to a predisposition for the emergence of aggressive behavior (78). Furthermore, it has also been suggested that low cholesterol might be accompanied by a decrease in plasma levels of the serotonin precursor tryptophan (76,77). Overall, there is a consistent body of evidence showing that decreased serum cholesterol levels are associated with a central serotonergic hypofunction, resulting in aggressive traits, which might involve suicidal behavior as a self-directed aggressive behavior.

**Serum lipid studies in suicidal patients**

An understanding of the biologic correlates of the diathesis of suicide may provide a better opportunity for the prediction and prevention of suicidal behavior. Accordingly, it is imperative to demonstrate robust and reliable biomarkers of suicide risk in order to identify individuals at risk and provide appropriate timely interventions (5,63). Previous work revealed a relationship between low levels of circulating cholesterol and suicide risk, implicating serum cholesterol level as one such potential biomarker, but the underpinnings of this relationship remain mostly unknown (22,71,79-85). In a recent meta-analysis conducted by Wu et al. that included 65 studies with a total of 510,392 participants, it was found that suicidal patients had significantly decreased levels of serum total

cholesterol compared with the non-suicidal patients (weighted mean difference [WMD] -22.35, 95% confidence interval [CI]: -27.95 to -16.75), LDL cholesterol (WMD -19.56, 95% CI: -26.13 to -12.99) and triglyceride (WMD -23.40, 95% CI: -32.38 to -14.42), and compared with healthy counterparts, patients with suicidal behavior had significantly lower total cholesterol (WMD -24.75, 95% CI: -27.71 to -21.78), HDL cholesterol (WMD -1.75, 95% CI: -3.01 to -0.48) and LDL cholesterol (WMD -3.85, 95% CI: -7.45 to -0.26) levels (86). The authors, however, highlighted that there was extremely high heterogeneity across the studies. In particular, subjects with mood disorders under statin treatment had an almost three-fold increase in rates of suicidal ideation, but no association with dietary patterns was identified (87). Impulsive behaviors that might contribute to more violent patterns of suicidal behavior have also been associated with the lipid profile (35,84,85,88-90); thus, low serum cholesterol might be involved, particularly in violent suicide attempts (91,92).

Despite some methodologic limitations, possible neurochemical links between suicide attempts and reduced levels of serum cholesterol have been postulated where a decrease in the cholesterol content of the lipid rafts of synaptic membranes might lead to reduced serotonergic neurotransmission (41,93), which is involved in impulsive and suicidal behaviors (91). It has been suggested that a decrease of serum cholesterol levels might involve changes in the viscosity of the cellular membranes and reduced functioning of serotonin receptors and transporters, which is closely associated with impulsivity and suicidal ideation (89). Despite numerous genome-wide association studies of suicidal behavior reporting inconsistent results (94), Knowles et al. identified a region on 2p25 containing the ACP1 gene, which was linked to the risk for attempted suicide (95). The ACP1 gene is in relation with cholesterol metabolism and transport, and Knowles et al. suggested that there may be a genetic overlap between the metabolism of esterified and total cholesterol and risk of suicidal behavior. Although much work has established an association between serum lipids and suicidal behavior, a few studies were unable to demonstrate such a relationship. For instance, Park et al. reported no association between low serum cholesterol levels and the presence of suicide attempts in patients with major affective disorders (96). In addition, Fiedorowicz et al. reported that low serum cholesterol levels did not predict subsequent suicide attempts in a prospective sample of inpatients with unipolar major depression, bipolar depression or

schizoaffective depression (97). Pompili et al. found no significant difference in serum cholesterol and triglyceride levels between patients with major affective disorders who had been admitted for a medically serious suicide attempt and non-suicidal patients (98). The disparity in findings yielded from various studies may be a result of the diagnostic heterogeneity of study samples and the variability of definitions and classification schemes for suicidal behavior.

<center>**Table 2 to be inserted here**</center>

**Discussion**

Impulsivity and aggression are well-established traits of suicidal behavior; however, there are substantial challenges in defining and stratifying both dimensions, and operational definitions of both constructs vary considerably. Therefore, there is a need for a clearer conceptual refinement for both impulsivity and aggression. Beyond such conceptualization challenges, it has been well documented that there is much psychological and biological overlap between impulsivity and aggression (13). For instance, there is a growing consensus that impulsivity is heterogeneous and should not be considered a unitary construct, instead it reflects a multi-faceted variety of behaviors and cognitive processes, whereas aggression represents both state and trait dimensions including complex emotional, cognitive, and behavioral processes (99). The neuropsychological processes of both constructs are regulated by similar neural circuits involving prefrontal limbic structures and the amygdala (5). The importance of understanding the relationship between impulsivity and aggression lies in the fact that there is a significant involvement of both constructs in the emergence of suicidal behavior. Thus, understanding the neurobiologic substrates of both constructs is imperative to identifying possible biomarkers of suicide risk, which may allow us to provide appropriate and immediate interventions to at-risk populations.

The certain neural mechanism by which impulsivity and aggression interacts with the underlying psychopathology thus producing suicidal behavior still remains elusive. According to the most prominent postulation, a central hypofunctional serotonergic neurotransmission is associated with impulsive aggression, which leads to suicidal behavior (15). Besides neuroimaging and postmortem studies (5), the neurobiologic underpinnings of the hyposerotonergic state have been examined in the

context of the serotonin–cholesterol relationship (93). Numerous types of lipid fractions are involved in substantial cellular functions such as membrane composition, energy storage, and signal transduction (100). Moreover, cholesterol provides maintenance of plasma membrane fluidity, neurogenesis, and transmembrane protein and receptor activity in neurons (18,101,102). Therefore, changes in cholesterol metabolism may significantly modulate brain-related functions. From this perspective, the role of lipids in neuronal functions has been acknowledged in many psychiatric entities including MDD, which has been linked with low serum and central cholesterol levels (103,104). Although low cholesterol levels have been associated with suicidal behavior (86,105), Kuwano et al. showed that levels of serum cholesteryl esters (CE) were negatively correlated with motivational symptoms including suicidal thoughts, which might indicate cognitive aspects of suicidal behavior are also related with low lipidergic fraction levels (106).

Despite the well-demonstrated biologic significance of lipid subtypes in neuronal functions, much remains unknown regarding the involvement of lipids in the pathophysiology of impulsivity, aggression, and suicide attempts in the context of serotonin–cholesterol hypothesis. The essential amino acid tryptophan serves as a precursor of serotonin along the enzymatic cascade called the tryptophan–kynurenine pathway (107). Abnormalities of the tryptophan–kynurenine pathway lead to decreased serotonin synthesis and release, and increased levels of neurotoxic kynurenine compounds such as quinolinic acid, all of which are associated with MDD, suicidal behavior, impulsivity, and aggression (107-117). The over-activation of tryptophan 2,3-dioxygenase (TDO) and indoleamine 2,3-dioxygenase (IDO), which degrades tryptophan to kynurenine along this pathway, is suggested to reduce serotonin synthesis through the upregulation of tryptophan degradation, and such imbalance of the tryptophan–kynurenine pathway is suggested to be involved in the development of depression (108,110,118). In addition, proinflammatory cytokines such as interleukin (IL)-6 and tumor necrosis factor (TNF)-α are known to activate IDO, which inhibits biosynthesis from tryptophan to serotonin (108,114,118,119). Increased inflammatory tonus, which has been associated with MDD, suicidal behavior, and aggression (109,120,121), causes a disruption in the tryptophan–kynurenine pathway in which lipid metabolism may be involved. In this regard, it has been demonstrated that serotonin deficiency is caused by elevated

oxidative stress associated with the altered metabolism of serum lipid fractions in tryptophan hydroxylase-2 knockout mice (122). In addition, it has been hypothesized that altered levels of peripheral lipid subtypes may be linked with increased neurotoxic tryptophan metabolites in the pathophysiology of MDD (106). A negative correlation has also been found between plasma kynurenic acid, which has neuroprotective properties, and the vegetative symptoms related to suicidal thoughts (106). In addition, the genetic overlap between lipid metabolism and suicidal behavior risk may also be the focus of future research, particularly within the context of the relationship between cholesterol metabolism and suicidal behavior (95).

In conclusion, the well-established association between aggression, impulsivity, and suicidal behavior has been based on decades of research and clinical practice. Nonetheless, relevant literature presents insufficient evidence on the neurobiologic underpinnings of such an association. This is probably due to difficulties in conceptualization and the operational definitions of impulsivity and aggression in the context of suicide. The burgeoning literature considering the neurobiologic substrates of both personality domains may aid in achieving the conceptualization of impulsivity and aggression, and in yielding a better understanding of the pathophysiology of suicidal behavior. More comprehensive examinations of both circulating and central lipid fractions including cholesterol may elucidate the neurochemical systems involved in the suicide-predisposing traits, impulsivity and aggression, which may lay the ground for identifying biomarkers that could be used to identify at-risk individuals to develop potential interventions to disrupt the pathogenesis of suicidal behavior.

## Acknowledgements

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**Box 1:** Search strategy and selection criteria

For this narrative review, an electronic database search was performed using different combinations of relevant keywords including *suicide, suicidal behavior, impulsivity, aggression, neurobiology, lipids, cholesterol* and *serotonin*. Both preclinical and clinical studies published between 1980 and 2020 matching the scope of this article were reviewed and filtered through an inspection of the abstracts to recruit the most suitable articles that contributed essential and substantial findings to the literature in order to space considerations.

**Table 2:** Important findings of recent studies on lipid profile in suicidal populations over the last two decades.

| Authors and year | Subjects | Methods | Major Findings |
|---|---|---|---|
| Lee and Kim (2003) (123) | 60 patients with suicide attempts vs. health controls | Serum lipid profiles, Weisman and Worden's risk-rescue rating scale | Low serum cholesterol could be a potential biological marker for assessing the risk of suicide. |
| Brunner et al. (2006) (124) | A meta-analysis of 4,181 subjects (18–65 years) | Serum lipids | This study is consistent with a positive relationship between cholesterol and completed suicide. |
| Bartoli et al. (2016) (125) | 214 inpatients with major depressive disorder | Serum lipids | No relationship between serum lipids and suicide attempt; serum lipids do not differentiate between violent and non-violent suicide attempts |
| Knowles et al. (2018) (95) | Comprising a total of 1897 individuals from 96 pedigrees | Serum total cholesterol, combination of bivariate polygenic and coefficient-of-relatedness analysis | Total cholesterol has significant genetic overlap with risk for suicide attempts |
| Ayese-Arriola et al. (2018) (126) | First-episode psychosis sample (N=383) | Lipid profile | The lipid profile test can be considered as a biological marker in the assessment of suicide risk in psychosis. |
| Mathew et al. (2018) (41) | attempted suicide patients (n=12) vs. healthy controls (n=10). | Plasma esterified cholesterol, fluorescence anisotropy, estimated flow activation energy | Decreasing membrane fluidity may disrupt the serotonergic neurotransmission involved in the pathophysiology of suicide. |
| Suneson et al. (2019) (84) | 52 drug-naive inpatients with suicide attempts | Serum lipids, Comprehensive Psychopathological Rating Scale, Karolinska Scales of Personality | Low total cholesterol is associated with higher levels of aggression in suicide attempters |
| Aguglia et al. (2019) (85) | 133 high-lethal and 299 low-lethal suicide attempters, 200 non-attempters | Serum lipids, CRP, and thyroid function tests | Low serum total cholesterol is associated with increase in the risk of high-lethal suicide attempt |
| Chen et al. (2019) (79) | Case-control study of 41 cases of suicide deaths | Serum total cholesterol | A low serum total cholesterol level is associated with an increased risk of a suicide death. |