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Relationship between blood cholesterol and suicidal behaviour

Abstract. *According to the World Health Organization report for 2021, the Republic of Kazakhstan is among the countries with a high suicide rate in the world ranking, ranking 20th. The nature and mechanisms of the development of suicidal behaviour in humans continue to be insufficiently clear. Previously, a number of studies have revealed the relationship between the level of lipids, in particular cholesterol, and the development of suicidal behaviour. Along with this, there are studies that have not revealed any connection between suicidal behaviour and cholesterol levels. Consequently, the role of cholesterol in the development of suicidal behaviour in humans is an interesting research question. In this regard, we conducted a literature review to determine the relationship between blood cholesterol levels and suicidal behaviour. The literature was searched in the databases Web of Science, PubMed, Scopus, and eLibrary. The search was carried out by the keywords: "cholesterol" or "total cholesterol" and "suicide" or "suicidal behaviour". Articles in English and Russian were included. Studies involving only adult patients were included. As a result of the analysis of 79 articles, it was revealed that the majority of authors (70%) came to the conclusion confirming the relationship between cholesterol levels and suicidal behaviour. However, there are a number of studies that do not confirm the existence of such a connection (17%). Despite the revealed contrast, there is a small part of the works (13%) that are presented by reviews and meta-analyses and cannot give an unambiguous answer to the research question we are interested in. Thus, the revealed contradictions can be explained by the fact that suicidal behaviour is complex and multifactorial. The use of cholesterol levels as a biomarker in the future would allow clinicians to obtain a laboratory marker, which, in combination with clinical assessments and symptoms, can make it possible to make a timelier diagnosis and assess the risks in patients with suicidal behaviour. However, to date, the mechanisms of this relationship remain unclear, which is the field for further scientific activity.*
Keywords: *cholesterol, suicide, self-harming behaviour.*

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Introduction

In recent years, according to the Committee on Legal Statistics and Special Accounts of the Prosecutor General's Office of the Republic of Kazakhstan, there is a tendency to decrease suicidal behaviour in Kazakhstan. Thus, in 2021, 4thousand people committed suicide in the country. In 2022, this figure decreased to 3.7 thousand people. Despite this, according to the World Health Organization report for 2021, our country is among the countries with a high suicide rate in the world ranking, ranking 20th. According to the reports of the group of experts for the United Nations Children's Fund (UNICEF) over the past ten years, the number of suicides in the Republic of Kazakhstan amounted to 52-53 per 100 thousand population, with a critical suicide threshold of over 20 people per 100 thousand population. In fact, the figures are even

higher, since a huge number of suicides are hidden behind other causes of death, such as road accidents or accidental poisoning. The presented statistics of commited suicides reflect the scale of the problem only partially. The ratio of completed suicides, suicide attempts and trends are on average 1:10:100. In our country, 4.5 thousand people attempted suicide in 2021, and 3.7 thousand people in 2022. The above statistics confirm the special relevance of this problem for our country. Since the nature and mechanisms of the development of suicidal behaviour in humans continue to be insufficiently clear, further research in this area is needed.

Previously, a number of studies have revealed the relationship between the level of lipids, in particular cholesterol (hereinafter referred to as CH) and the development of suicidal behaviour [1, 2, 3, 4, 5, 6, 7]. The first mention of this relationship was noted in 1990 in a meta-analysis of primary intervention studies in cardiovascular diseases, which showed that cholesterol-lowering treatment leads to an increase in mortality from diseases, mainly from suicides and injuries [8]. Along with this, there are studies that have not revealed any connection between suicidal behaviour and cholesterol levels [9, 10, 11, 12, 13, 14]. Therefore, the role of cholesterol in the development of suicidal behaviour in humans is an interesting research question and may be a promising direction in the study of this problem.

In this regard, the purpose of this article is to review the literature on the role of cholesterol levels in the development of suicidal behaviour.

Methodology

Literature search was conducted in the databases Web of Science, PubMed, Scopus. The search was carried out by the keywords: "cholesterol" OR "total cholesterol" and "suicide" OR "suicidal behaviour." The literature search yielded 190 results, of which 156 articles. This topic has been sanctified since 1990 [8]. The question has become more and more relevant over time. And the largest number of articles falls on 2017 and 2018 (17 and 16 articles, respectively). Articles in English and Russian were included. This review included studies involving only adult patients. 79 articles were selected.

Results

As a result of the analysis of 79 articles, it was revealed that the majority of authors (70%) came to the conclusion confirming the relationship between cholesterol levels and suicidal behaviour. Along with this, there are a number of studies that do not confirm the existence of such a connection (17%). Despite the revealed contrast, there is a small part of the works (13%) that are presented by reviews and meta-analyses and do not have an unambiguous answer to the research question we are interested in. Thus, the revealed contradictions can be explained by the fact that suicidal behaviour is a complex and multifactorial phenomenon. We grouped and divided the authors' information into 3 groups: CH affects suicidal behaviour; CH does not affect suicidal behaviour and a neutral position.

Authors	Year, country	Sample	Comment
Cholesterol affects suicidal behaviour			
Danbaev S.U.	2008, Kazakhstan	3565 people	In young people, high suicidal activity is more often associated with low levels of cholesterol, in older age, increased cholesterol is a risk factor for atherosclerosis, which is also associated with increased suicidal activity.
Davidovsky S.V., Ibragimova Zh.A., etc.	2019, Belarus	160 people	The lowest values in the blood serum of men were noted in individuals who used high-lethal methods of self-harm.

Davidovsky S.V., Ibragimova Zh.A., etc.	2021, Belarus	224 people	In persons who have committed a suicide attempt, lower levels of TC and LDL in the blood serum were noted, regardless of gender.
Ainiyet B., Rybakowski J.K.	2014, Poland	148 people	In patients with depression, low levels of TC and LDL cholesterol, TG, and total lipids may be condition-dependent risk factors for suicidal behaviour.
Ainiyet B, Rybakowski J.K.	2014, Poland	223 people	A significant association was found between suicidal attempts and low levels of TC, LDL, and TG in patients with schizophrenia.
Mensi R., Messaoud A., Mhallah A., Azizi I.	2016, Tunisia	126 people	A decrease in CH was found in patients with schizophrenia with a recent suicide attempt, compared with patients with schizophrenia with long-standing suicides and a control group.
Messaoud A., Mensi R., Mrad A., Mhalla A. …	2017, Tunisia	313 people	For patients with depression, the level of cholesterol in blood plasma less than 3.47 mmol/l may indicate a possible risk of suicide.
Chen S., Mizoue T., Hu H., Kuwahara K. ...	2019, Japan	146619 people	In patients who committed suicide, the risk of suicide increased with a decrease in the level of CH for 3 years, before death.
Zhou S.Y., Zhao K., Shi X., Sun H.K. …	2021, Japan	580 people	In patients with severe depression, there was a decrease in TC, and higher levels of TG, LDL.
Segoviano-Mendoza M., Cardenas-de la Cruz M.…	2018, Mexico	261 people	There was a significant decrease in serum levels of TC, LDL, VLDL and TG in patients with depression and suicide attempts.
Aguglia A., Solano P. …	2019, Italy	632 people	A decrease in the level of CH was determined by 3-4 times in patients who committed suicide.
Ayesa-Arriola R., Canal Rivero M., Delgado-Alvarado M. …	2017, Spain	383 people	In patients after the first episode of depressive psychosis, it was noted that CH, LDL and depressive symptoms were largely associated with suicidal behaviour.
Horsten M., Wamala S.P., Vingerhoets A., Orth Gomer K.	1997, Sweden	300 people	Low CH levels in healthy middle-aged Swedish women were associated with a higher prevalence of depressive symptoms and a lack of social support.
Asellus P., Nordstrom P., Nordstrom A.L., Jokinen J.	2014, Sweden	81 people	We found a significant correlation between the manifestation of violence in childhood and the manifestation of violence, including towards oneself, in adulthood (i.e., the cycle of violence) only in the group with a CH level below the median.
Reddy A., Kalasapati L.K.	2020, India	98 people	In patients with suicidal attempts, nonviolent methods of suicidal attempts prevailed with elevated CH
Papadopoulou A., Markianos M. …	2013, Greece	51 people	There was a decrease in CH in patients after committing suicide attempts.

Emet M., Yucel A., Ozcan H., Gur S.T.A. …	2015, Turkey	284 people	In women after suicidal attempts, the levels of CH, LDL and TG were significantly lower in the suicidal group, and the level of HDL was significantly higher
Yagci I., Avci S.	2021, Turkey	91 people	The indicators of anxiety, depression and suicidal thoughts were higher in the experimental group. In addition, vitamin D, CH and TG levels were significantly lower.
Daray F.M., Mann J.J., Sublette M.E.	2018, Argentina	125 sources	We suggest an association between low cholesterol, increased PUFA content from n-6 to n-3, decreased neurotransmission of 5-HT, inflammation and suicide risk.
Muldoon M.F., Manuck S.B., Matthews K.A.	1990, USA	24847 people	The first mention of the relationship was when it was noted that cholesterol-lowering treatment leads to an increase in mortality mainly from suicides and injuries
Fiedorowicz J.G., Coryell W.H.	2007, USA	74 people	Patients with high levels of CH were associated with an increased risk of suicide attempts in the analysis of survival in people younger than middle age suffering from mental illness
Coryell W., Schlesser M.	2007, USA	75 people	The decrease in CH reflects the risk of violence and suicidal thoughts in patients
Reuter C., Caldwell B., Basehore H.	2017, USA	128 people	Suicidal veterans were younger, slimmer and had more anxiety, sleep problems and higher education, had a reduced level of CH.
Garland M., Hickey D., Corvin A., Golden J., Fitzpatrick P. …	2000, Ireland	200 people	The reported increased mortality in low-CH populations may be due to an increase in the number of suicides and accidents caused by an increased propensity for impulsivity in these populations.
Ma Y.J., Wang D.F., Yuan M., Zhang X.J., Long J. …	2019, China	288 people	In patients with the first episode of severe depressive disorder, high levels of CH may be a consequence of suicide attempts and severe depression
Li H., Zhang X.Y., Sun Q., Zou R., Li Z.J., Liu S.Y.	2020, China	32 sources	It was demonstrated that lower concentrations of TC and LDL cholesterol, but not HDL and TG, were associated with suicide attempts in patients with depression.
Ma Y.J., Zhou Y.J., Wang D.F., Li Y., Wang D.M. …	2020, China	1718 people	At an early stage, patients with depression have low CH and more serious symptoms of anxiety and depression correlate with suicide attempts.
Shrivastava A., Johnston M., Campbell R., De Sousa A. ...	2017, Canada	60 people	The study suggests lower CH in psychotic patients with severe suicidal thoughts and depression in the early stages of psychosis.
Zureik M., Courbon D., Ducimetiere P.	1996, France	6393 people	A study of completed suicides in a large sample of patients over 17 years confirms the link with a decrease in the level of CH

Dimeny E., Ban E., Fekete L.G., Brassai A.	2021, Romania	200 people	In patients with schizophrenia, a link was found between suicidal thoughts and low levels of TC, LDL, TG in patients of both sexes.
Sankaranarayanan A., Jenkins Z. …	2020, Australia	28 sources	It is noted that a decrease in CH can serve as a marker of the risk of violence and suicidal tendencies in psychiatric patients with schizophrenia
Cholesterol does NOT affect suicidal behaviour			
D'Ambrosio V., Salvi V., Bogetto F., Maina G.	2012, Italy	220 people	Clinical parameters played an important role in the development of suicidal behaviour (gender, low level of education, more mania and depression, taking more medications).
Bartoli F., Crocamo C., Dakanalis A. …	2017, Italy	214 people	They do not confirm the hypothesis that CH and suicide attempts are associated in patients with severe depressive disorder.
Capuzzi E., Bartoli F., Crocamo C., Malerba M.R. …	2018, Italy	593 people	The link between the lipid profile and suicide attempts in people with mental disorders has not been fully confirmed.
Cantarelli M.D., Nardin P., Buffon A., Eidt M.C. …	2014, Brazil	86 people	In patients with affective disorders, there was a decrease in BMI, OT, TG in patients after suicidal attempts
Vartiainen E., Puska P., Pekkanen J., Tuomilehto J., Lonnqvist J., Ehnholm C.	1994, Finland	22432 people	The risk of accidents, suicides and other violent deaths was not associated with the concentration of CH in the blood serum, whereas such deaths were more common in smokers and alcohol users.
Zhao K., Zhou S.Y., Shi X., Chen J.J. …	2020, China	740 people	Having studied young patients with depression, they did not find a connection with the level of CH, but they found a relationship with the level of HDL and glucose
Park S., Yi K.K., Na R., Lim A., Hong J.P.	2013, South Korea	596 people	The level of TG is associated with suicidal behaviour when BMI, TC, LDL, HDL and VLDL did not matter.
Park Y.M., Lee B.H., Lee S.H.	2014, South Korea	73 people	Revealed the relationship between TG and suicidal thoughts, which does not depend on both BMI and body weight.
Lalovic A., Levy E., Luheshi G., Canetti L., Grenier E., Sequeira A., Turecki G.	2007, Canada	62 people	No connection was found. However, depending on the method of death, it was found that in violent suicides, the content of HC in the gray matter is generally lower, especially in the frontal cortex
Neutral position			
Razvedovsky Yu. E.	2021, Belarus	46 sources	The gender aspect of the relationship between dyslipidemia and suicidal behaviour remains insufficiently developed, since most studies on this problem were carried out with the participation of men.

Sen P., Adewusi D., Blakemore A.I., Kumari V.	2021 Great Britain	23 sources	In patients with schizophrenia, the authors found a link between low cholesterol and suicidal behaviour, only in half of the studies.
Kulak-Bejda A., Bejda G., Lech M.	2021, Poland	66 sources	Conflicting results have been reported.
Troisi A.	2009, Italy	76 sources	It is obvious that there are some subgroups of vulnerable people who, unlike most people in the general population, are subject to adverse psychological and behavioural consequences associated with low levels of cholesterol.
Conroy R.M.	1993, Ireland	30 sources	On a practical level, patients receiving cholesterol-lowering therapy should be warned about the need to control the mood of such patients.
Muldoon M.F., Manuck S.B., Mendelsohn A.B., Kaplan J.R., Belle S.H.	2001, USA	19 sources	Currently available data do not indicate that cholesterol-lowering treatment significantly increases suicidal mortality.
Gokcay H. Balcioglu Y.H.	2020, Turkey	98 sources	In patients treated with statins, the frequency of suicidal thoughts increased, but no connection was found with dietary characteristics

Abbreviations:

CH – cholesterol
TC – total cholesterol
HDL – high-density lipoproteins
LDL – low-density lipoproteins
VLDL – very low density lipoproteins
TG – triglycerides
PUFA – polyunsaturated fatty acids
BMI – body mass index

Discussion

Cholesterol affects suicidal behaviour:

Most of the authors have identified the presence of a relationship between the level of blood cholesterol and suicidal behaviour of a person [2, 4, 5, 6]. A study of a large sample of patients from 2013 to 2018 determined a 3-4–fold decrease in the level of CH in patients who committed suicide compared to the control group [15]. A large study of completed suicides conducted on a large sample of patients over 17 years confirms the association with a decrease in the level of CH [16]. Japanese scientists, retrospectively examining a group of patients who committed suicide, came to the conclusion that the risk of suicide increased with a decrease in the level of CH for 3 years, before death. In this study, a decrease in mean CH by 0.5 mmol/l was associated with an 18% increase in the risk of suicide [17].

Despite the available information about the presence of a link between low CH in the blood serum and suicide, the mechanism of the link between lipids and suicidality itself still remains unclear. It is well known that cholesterol, as a vital component of the cell membranes of higher eukaryotes, plays a major role in the functioning and organization of membranes. Basically,

CH is dispersed in a certain order in specialized regions (domains) in membranes [18]. Thus, these areas are called "lipid rafts" [19], they are the foundation for preserving the structure and function of the membrane. Earlier it became known that almost all cholesterol in the brain is produced "insitu" by the synthesis of "denovo", meanwhile, the selectivity of the blood-brain barrier prevents its absorption from the bloodstream [20]. However, it is possible that a decrease in peripheral cholesterol in humans occurs together with modifications of cholesterol in different synaptic lipid rafts in neurons (using a common regulatory mechanism).

In the central nervous system, the neurotransmitter serotonin plays a key role in deterring aggressive behaviour. At the moment, there is a theory that describes the effect of serum cholesterol levels on decreased serotonergic activity of the brain. Thus, in the study, monkeys with experimentally reduced CH levels had higher concentrations of serotonin metabolites than monkeys who received a high-cholesterol diet. Consequently, a decrease in the activity of serotonergic communication leads to instinctive reactions and violent suicidal behaviour [21, 22].

There is also a theory that in lipid rafts, signals from a neurotransmitter can be transmitted through a certain group of receptors, such as the serotonin 1A (5-HT1A) receptor [23]. A number of studies have proved the need for the participation of membrane cholesterol in the functioning of the 5-HT1A receptor [24, 25, 26]. The results of another study showed that lipid fluidity regulates the binding of serotonin (5-HT) to a greater extent in the brain membranes of mice. Consequently, lowering cholesterol levels will increase the fluidity of the cell membrane [27].

There is also evidence that the disruption of rafts due to cholesterol reduction significantly reduces the binding of agonists and the binding of G-protein to serotonin receptors of 5-hydroxytryptamine 1A (5-HT1A) in the membranes of the hippocampus of cattle [23]. Not to mention the fact that serotonergic signaling is the most important in the organization and regulation of many neurofunctions, such as behavioural, cognitive and developmental brain function. Moreover, some studies have found a link between decreased 5-ht activity and suicide [21].

In addition, we note that a number of researchers have described the crystal structures of GPCR, including the serotonin 1A receptor, demonstrating evidence of cholesterol binding sites [28, 29]. At the moment, two possible options have been proposed for how membrane cholesterol affects the structure and function of GPCR. The first option: by specific interaction with GPCR. The second way -by changing the physical qualities of the membrane in which the receptor is embedded [30]. The aforementioned "cholesterol-serotonin" theory also takes place due to the fact that total cholesterol (hereinafter referred to as TC) deficiency provokes central neuroinflammation, thus affecting the serotonergic system, thereby increasing aggressiveness and impulsivity.

Along with this, CH plays an important role in membrane stability and neurotransmission, which include the transformation of the membrane lipid raft structure, due to the ratio of cholesterol and n-3 polyunsaturated fatty acids (hereinafter referred to as PUFA), which affect the activity of membrane-bound proteins such as serotonin receptors and transporters, as well as toll-like receptors [25]. Thus, low CH levels cause an increased n-6:n-3 PUFA ratio, therefore contributing to neuroinflammation, since n-3 PUFA exhibit anti-inflammatory properties, at the same time as n-6 PUFA levels exhibit pro-inflammatory activity and disinhibit two inflammatory processes [31]. According to some researchers, abnormal monoaminergic neurotransmission along with neuroinflammation are the leading biological factors underlying suicidal behaviour [32]. Some studies have associated hypercholesterolemia with depression in mice through monoaminergic metabolism. They reported higher monoamine oxidase (MAO) activity A and B in the hippocampus of mice [33].

Therefore, this is a possible reason that high cholesterol levels can cause depression in much the same way as low levels. Also recently, researchers have put forward an interesting hypothesis about the existence of a connection between the well-known process of cholesterol metabolism, as well as the neurobiological basis of suicide risk, through the ability to remove cholesterol specific to ABCA1 [34].

Other researchers have suggested that cholesterol influences suicidal behaviour due to the fact that it plays a leading role in the production of the myelin sheath, in transmembrane metabolism, the functioning of enzymes, in the synthesis of steroid hormones and the expression of neurotransmitter receptors [35].

Another researcher proposed a "diathesis-stress" model to explain the relationship between lipoproteins and suicidal behaviour [36]. The diathesis model suggests considering low lipid profile numbers as a sign associated with aggression and impulsivity, since they affect serotonergic transmission in the brain. Along with this, another possible version of the effect of lipids on suicidal behaviour is that leptin controls the dopamine response to characteristic stress stimuli not directly related to food [37].

A theory has also been put forward that low concentrations of peripheral lipids, changing the viscosity of membrane lipids in brain cells, thereby affecting synaptic plasticity, cause general brain dysfunction [27]. Previous studies have shown that the relationship between lipids and serotonin may have a basis at the genetic level, since in some patients with a connection with a short allele of polymorphism of the serotonin transporter gene and lower low-density lipoproteins (hereinafter referred to as LDL) concentrations [38]. Some researchers concluded that the relationship between serum cholesterol concentrations and suicidal behaviour in patients correlated with interleukin-2 and manifested itself at low CH concentrations and higher triglyceride concentrations [39], while other researchers found that cholesterol-lowering drugs can have an antidepressant effect through anti-inflammatory pathways [40]. There are studies in which researchers have suggested that the concentration of PUFA or the balance of omega-3 and omega-6 PUFA may play an important role in serotonergic function in suicidal behaviour [41]. There is also evidence that a lower total concentration of omega-3 fatty acids and an increased ratio of omega-6 and omega-3 can disrupt the biophysical properties of the neuronal membrane, therefore affect the uptake of serotonin, the binding of b2-adrenergic and serotonergic receptors with their respective ligands, as well as the activity of monoamine oxidase. [42].

Most often, patients suffering from depression are subject to suicidal behaviour. There is evidence that depressed patients after suicidal attempts have a lower level of CH than depressed patients without suicidal behaviour and patients without depression at all. As for the severity of depression, there were no significant changes in blood plasma lipid levels between mild, moderate and severe degrees of depression. Thus, for patients with depression, the level of CH in blood plasma less than 3.47 mmol/l may indicate a possible risk of suicide [4]. Other studies of patients with depression have revealed that there is a high risk of suicide in those patients who have lower levels of CH, LDL and more psychotic symptoms [1, 3]. In a study with a large sample of patients after the first episode of depressive psychosis, it was also noted that cholesterol, LDL and depressive symptoms were largely associated with suicidal behaviour. It was not possible to find a significant relationship between low concentrations of lipoproteins and more violent methods of suicide [43]. A study by Belarusian scientists emphasized that the lowest TC levels in blood serum were observed in men who used "high-lethal" methods of self-harm [44]. In a later study of the hormonal-metabolic status of individuals who have committed suicide, the same group of scientists noted lower levels of TC and LDL in blood serum, regardless of gender [45]. In addition, this study gives reason to believe that the mechanism of the relationship between cholesterol and suicidal behaviour is based on the inability to fully meet the needs of an organism under chronic stress, in particular, in the hormone cortisol, which is responsible for maintaining the metabolic balance of the body under stress. Since cholesterol is the initial substrate for the formation of cortisol in the cells of the adrenal cortex. The theory was put forward that the body's need for enhanced the formation of cortisol can affect an increase in the utilization of low- and high-density lipoprotein cholesterol from the blood, which can to some extent affect the content of total cholesterol in blood plasma and, consequently, in the structural formations of cell membranes (including the brain). Due to the low values of lipoprotein fractions and hypercortisolemia developed as a result of chronic stress, there is a violation of the state of plastic and energy metabolism in the body, which leads to a violation in the system of

neurohumoral regulation, represented by the diencephalic region of the brain, therefore affecting the functioning of mental functions that control behaviour [45].Other researchers of patients with severe depression have revealed a decrease in TC, high–density lipoproteins (hereinafter - HDL) [46] and higher levels of triglycerides (hereinafter - TG), LDL [7]. However, Turkish scientists, studying women after suicidal attempts, came to the conclusion that the levels of CH, LDL and TG were significantly lower in the suicidal group, and the level of HDL was significantly higher [47].In a Stockholm study of healthy women, it was noted that if the serum cholesterol was less than 4.7 mmol/l, then depressive symptoms were noted. And in the absence of social support, a low level of CH in the future leads to depression and then to suicide [48].

Patients diagnosed with schizophrenia also often have a high risk of developing suicidal behaviour. With the help of the study, a decrease in cholesterol was found in patients with schizophrenia with a recent suicide attempt, compared with patients with schizophrenia with long-standing suicides and a control group. It is also noted that suicidal behaviour is more characteristic of paranoid schizophrenia [49]. Examining patients with schizophrenia alone, a significant association was found between suicidal thoughts, suicidal attempts and low levels of TC, LDL, TG and total lipids in both male and female patients [50, 51]. It has been suggested that ethnic differences may play a role in the presence or absence of this relationship [50]. A meta-analysis [52], a literature review [53] and studies on patients with schizophrenia also note that a decrease in CH can serve as a biological marker of the risk of violence and suicidal tendencies in psychiatric patients [54].

There are articles in which the authors came to the conclusion that not only cholesterol affects suicidal behaviour. For example, in patients after suicidal attempts, not only CH and TG, but also vitamin D levels were significantly lower than in the control group [55]. The authors of the literature review suggest a relationship between low cholesterol, high content of polyunsaturated fatty acids, inflammation and suicide risk [56]. Scientists from Japan noted in their study that people who committed suicide had higher blood glucose levels than in the control group [17]. A significant increase in non-disease-related deaths (deaths from accidents, suicide or violence) was found in the groups treated to reduce the concentration of HC compared to the control group [8]. The authors of one study made an interesting assumption that people who experienced violence in childhood with a reduced level of CH have a higher risk of developing suicidal behaviour [57].Some authors suggest that the increased mortality of the population with a low level of CH may be caused by an increased tendency to impulsivity in these population groups and especially if they used violent methods to commit suicide [58, 59, 60]. The results of other authors also show that a low level of CS is associated with aggression in people trying to commit suicide [61, 62]. In a study of Vietnam War veterans, it is reported that patients who have suicidal thoughts or attempts have a significant decrease in the level of CH. In addition, they were younger, slimmer and had more worries, sleep problems [63].

While most researchers tend to believe that low CH affects suicidal behaviour, on the contrary, there are works that have noted the connection of suicidal behaviour with high levels of cholesterol. In a Japanese study with a large number of participants, it was noted that women with high TC and LDL had a high risk of suicide [64]. Also, the authors who studied patients with the first episode of severe depressive disorder concluded that a high level of CH may be a consequence of suicide attempts and severe depression [65]. Researchers have put forward several possible mechanisms of association between hypercholesterolemia and the risk of suicidal behaviour. It is described that people with high cholesterol are prone to maladaptive eating behaviour (overeating), which may be one of the symptoms of depression, which is a risk factor for suicide [65]. It is also assumed that this relationship is explained by the fact that the atherogenic lipid profile increases the likelihood of stroke, which in turn increases the risk of suicidal behaviour [64]. Abnormal lipid profile may also be a sign of other metabolic disorders associated with an increased risk of suicidal behaviour. One of the mediators of the relationship between lipids and suicidal activity are omega-3 polyunsaturated fatty acids, the low level of which is associated with depression and suicidal behaviour [64]. It is also assumed

that hypercholesterolemia increases the activity of monoamine oxidase (MAO) types A and B, thus increasing the risk of depression, which in turn is a risk factor for suicidal behaviour [66]. Another group of scientists found that patients with high levels of CH were associated with an increased risk of suicide attempts when analyzing survival in people younger than middle age suffering from mental illness [66]. Examining patients with suicidal attempts, a link was found with a decrease in CH, and nonviolent methods of parasuicide prevailed at elevated levels of CH [67, 68]. Domestic researchers who observed 3,565 residents in the East Kazakhstan region for 4 years determined that the risk of suicide in people under 30 years of age increases with low levels of cholesterol in the blood. When, at the age of more than 50 years, the risk of suicide increases at high concentrations of CH [69].

Cholesterol does NOT affect suicidal behaviour

However, there are a number of studies that have not confirmed the link between the level of CH and suicidal behaviour. Many authors who studied patients with mental disorders, including after suicidal attempts, did not find a relationship with the level of CH [9, 10, 11, 12, 14, 70]. In patients with bipolar disorder, clinical characteristics such as gender, low level of education, more manic and depressive episodes and taking more medications played an important role in the development of suicidal behaviour [12].

In a study of patients with affective disorders, a decrease in body mass index (hereinafter referred to as BMI), waist circumference and TG was noted in patients after suicidal attempts [10]. Other authors also concluded that the level of TG is associated with suicidal behaviour, while BMI, TC, LDL, HDL and very low density lipoproteins (hereinafter referred to as VLDL) did not matter [70]. A study focused on young patients with depression did not show a link with the level of cholesterol, but found a relationship with HDL and glucose levels [14].

The results of the study, which studied completed suicides in patients with severe mental disorders, also found no relationship with the level of blood cholesterol [13]. A large cohort study conducted from 1972 to 1977 in Finland examined completed suicides and other violent deaths. The risk of accidents, suicides and other violent deaths was not associated with the concentration of CH in the blood serum, but such deaths were more common in smokers and alcohol users [71]. When studying the content of CH in the frontal cortex, amygdala or hippocampus in individuals who committed suicide, no differences were found compared with the control group. However, when suicide participants were divided into violent or nonviolent groups depending on the method of death, it was found that in violent suicides the content of CH in the gray matter was generally lower than in nonviolent, especially in the frontal cortex [72].

Neutral position

A small number of papers presented by reviews and meta-analyses have come to contradictory results [73, 74]. According to a systematic review involving patients with schizophrenia, the authors found a link between low cholesterol and suicidal behaviour in about half of the studies [75]. Similarly, a literature review conducted by Troisi A. it reflects contradictory data, and therefore, it becomes obvious to the author that there are certain subgroups of vulnerable people who, unlike most people in the general population, are subject to adverse psychological and behavioural consequences associated with a low level of CH [76]. The authors of another literature review, who have covered the literature for 40 years, found more evidence of the existence of a connection, but still could not miss the contradictions [77]. There is conflicting information about the role of statins in suicidal behaviour. Several authors note that in patients treated with statins, the frequency of suicidal thoughts increased, but no connection was found with dietary habits, diets [77, 78]. In a meta-analysis that studied methods of reducing cholesterol and the relationship with suicide, it was noted that statins do not affect suicide in any way, unlike nutrition [79].

Conclusion

As a result of the literature review, we received contradictory information. However, more than half of the analyzed studies (70%) confirm the existence of a relationship between cholesterol levels and suicidal behaviour. The use of cholesterol levels as a biomarker in the future would allow clinicians to obtain a laboratory result, which, in combination with clinical assessments and symptoms, may allow for a more timely diagnosis and assessment of risks in patients with suicidal behaviour. To date, the mechanisms of the studied relationship are still unclear, which is the field for further scientific activity.

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Қан холестеринімен суицидтік мінез-құлық арасындағы байланыс

Аңдатпа. *ДДҰ* (*Дүниежүзілік Денсаулық сақтау ұйымы*) 2021 жылғы есебіне сәйкес, біздің еліміз әлемдік рейтингте суицид деңгейі жоғары елдердің қатарына кіріп, 20-ші орынды алады. Адамдардағы суицидтік мінез–құлықты дамытудың табиғаты мен механизмдері әліде анық емес. Бұған дейін бір қатар жұмыстар *липидтердің* деңгейімен суицидтік мінез-құлықтың дамуы арасындағы байланысты анықтады. Сонымен қатар, суицидтік мінез-құлықтың холестерин деңгейімен ешқандай байланысы жоқ деректерде бар. *Демек*, холестериннің адамдағы суицидтік мінез-құлықты дамытудағы рөлі қызықты зерттеу мәселесі болып табылады. Осыған байланысты біз холестерин деңгейімен суицидтік мінез-құлық арасындағы байланысты анықтау үшін әдебиеттерге шолу жасадық. Әдебиеттерді іздеу Web of Science, PubMed, Scopus, eLibrary дерек қорларында жүргізілді. Іздеу «холестерин» немесе «жалпы холестерин» және «суицид» немесе «суицидтік мінез-құлық» кілт сөздері бойынша анықталды. Ағылшын және орыс тілдеріндегі мақалалар енгізіліп, тек ересек пациенттер қатысқан зерттеулер қамтылды. 79 мақаланы талдау нәтижесінде авторлардың көпшілігі (70%) холестерин деңгейімен суицидтік мінез-құлық арасындағы байланысты растайтын қорытындыға келгені анықталды. Алайда, мұндай байланыстың болуын растамайтын бір қатар зерттеулерде бар (17%). Анықталған қарама-қайшылыққа қарамастан, жұмыстың аз бөлігі (13%) шолулармен ұсынылған және бізді қызықтыратын зерттеу сұрағына нақты жауап бере алмайды. Осылайша, анықталған қарама-қайшылықтарды суицидтік мінез-құлықтың күрделі және көпфакторлы екендігімен түсіндіруге болады. Болашақта холестерин деңгейін биомаркер ретінде пайдалану зертханалық маркерді алуға мүмкіндік береді, ол клиникалық бағалаулармен және белгілермен бірге суицидтік мінез-құлқы бар науқастарда уақтылы диагноз қоюға және тәуекелдерді бағалауға мүмкіндік береді. Алайда, бүгінгі күні бұл қатынастың механизмдері түсініксіз болып тұр, бұл одан әрі ғылыми іздестірудің қажеттілігін білдіреді.

Түйін сөздер: холестерин, суицид, өзіне зиян келтіретін мінез-құлық.

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Взаимосвязь уровня холестерина крови и суицидального поведения

Аннотация. Согласно отчету ВОЗ (Всемирная организация здравоохранения) за 2021 г, Республика Казахстан входит в число стран с высоким уровнем суицидов в мировом рейтинге, занимая 20 место. Природа и механизмы развития суицидального поведения у людей продолжают оставаться недостаточно ясными. Ранее ряд работ выявил взаимосвязь между уровнем *липидов*, в частности, холестерина и развитием суицидального поведения. Наряду с этим имеются работы, которые не выявили никакой связи суицидального поведения с уровнем холестерина. Следовательно, роль холестерина в развитии суицидального поведения у человека представляется интересным исследовательским вопросом. В связи с этим мы провели обзор *литературы для* определения взаимосвязи между уровнем холестерина крови и суицидальным поведением. Поиск *литературы* проводился в базах данных Web of Science, PubMed, Scopus, eLibrary. Поиск проводился по ключевым словам: “холестерин” или “общий холестерин” и “суицид” или “суицидальное поведение”. Были включены статьи на английском и русском языках. Включались исследования, где участвовали только взрослые пациенты. В результате анализа 79 статей было выявлено, что большинство авторов (70%) пришли к выводу, подтверждающему взаимосвязь между уровнем холестерина и суицидальным поведением. Однако имеется ряд исследований, которые не подтверждают наличие такой связи (17%). Несмотря на выявленный контраст, имеется небольшая часть работ (13%), которые представлены обзорами и метаанализами и не могут дать однозначного ответа на интересующий нас исследовательский вопрос. Таким образом, выявленные противоречия можно объяснить

тем, что суицидальное поведение является сложным и многофакторным. Использование уровня холестерина в качестве биомаркера в будущем позволило бы клиницистам получить лабораторный маркер, который в сочетании с клиническими оценками и симптомами может позволить поставить более своевременный диагноз и оценить риски у пациентов с суицидальным поведением. Однако на сегодняшний день механизмы данной взаимосвязи остаются неясными, что представляет поле для дальнейшей научной деятельности.

Ключевые слова: холестерин, самоубийство, самоповреждающее поведение.

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