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Brain and Stunting: Integrative Clinical and Community Stunting Prevention Perspectives in Disorders of Brain Development

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Abstract

Stunting is a health problem that is very urgent to be addressed. This is associated with increased morbidity, mortality, development of cognitive impairment and an increased risk of various chronic diseases in the future. The research method uses a qualitative approach. With the literature review method, which includes activities related to library data collection methods, reading and recording, and managing research materials. The results of the study show that the treatment of stunting can be divided into 2 methods. First, specific interventions that contribute 30% to the success of treatment, are aimed at children within the First 1,000 Days of Life (HPK), are generally carried out by the health sector and are short-term in nature. This can be done through the target group of adolescents and women of childbearing age, pregnant women, nursing mothers and children 0-23 months, children 24-59 months through priority, important and conditional interventions. The two sensitive interventions, which contribute 70%, are aimed at various development activities outside the health sector targeting the general public. The types of interventions that can be carried out are increasing the supply of drinking water and sanitation, increasing access to and quality of nutrition and health services, increasing awareness, commitment, parenting practices, maternal and child nutrition, increasing access to nutritious food.

Keywords: Brain and Stunting, Clinical Integrative, Stunting Prevention

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Introduction

Global public health patterns have changed rapidly in recent decades. Medical science and technology are developing very rapidly, thus encouraging the discovery of new drugs and more effective ways of managing various diseases. This has resulted in an increase in life expectancy and a decrease in morbidity and mortality from infectious diseases. On the other hand, an increase in life expectancy is not necessarily accompanied by the adoption of a healthy lifestyle, resulting in an increase in the incidence of non-communicable diseases. “The Global Burden of Disease Study 2015” states that in the past quarter of a century there has been a shift in the pattern of neurological diseases, mortality and disability due to infectious diseases of the nervous system have decreased (Supantini, 2019).

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In practicing medicine, the majority of medical personnel work as clinicians in health facilities serving patients (individuals), so that what is prioritized is curative and rehabilitative health efforts. Preventive and promotive health efforts may be implemented but only in small proportions. Therefore, an innovative strategy is needed that can bridge programmable promotive-preventive health efforts in the community with curative-rehabilitative efforts carried out by clinicians on individuals, including preventing stunting in brain development disorders (Supantini, 2019).

Stunting is chronic malnutrition experienced by children during their growth and development. WHO defines stunting as a child aged 0-59 months who has a body length for age below two standard deviations (moderate and severe stunting), or three standard deviations (severe stunting) from the median value of the WHO growth curve. Stunting is still a global problem in the world, based on data from UNICEF and WHO, in 2018, there were 149 million children who were stunted. In Indonesia, the stunting rate based on the 2018 RISKESDAS was 30.8%, a decrease compared to 2013 data which reached 37.2%, but this figure is still relatively high. Factors that influence stunting in Indonesia include non-exclusive breastfeeding in the first 6 months, male gender, low socioeconomic status, premature birth, low birth length, and low education (Beal et al., 2018).

Figure 1. The prevalence of stunting (%) in various regions in Indonesia in children aged 0-59 months in 2013.2

Stunting is a health problem that is very important to address, because it is associated with increased morbidity, mortality, impaired cognitive development, and an increased risk of experiencing various chronic diseases in the future. Reducing stunting is the first point of the 6 targets of the 2025 Global Nutrition Target, and is a key indicator in the second Sustainable Development Goal of Zero hunger.2A healthy brain in childhood will result in a healthy brain in adulthood, with better levels of productivity, creativity and mental health.

Literature Reviews

Anormal Brain Development

The development of the human brain begins in the womb and continues until the postnatal period (after childbirth). To achieve a good development process, there are several factors that play an important role. In the prenatal period (in the womb), brain development is determined by genetic factors, maternal nutrition, and antenatal care. In the postnatal phase, factors that influence are nutrition, stimulation, a healthy environment, and care from the family.

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At 22 days after conception, the neural plate begins to bend inwards, forming the neural tube. In this period, the role of nutrition has begun to be seen. The formation of the neural plate and neural tube is influenced by folic acid, copper, and vitamin A. Seven weeks after conception, cell division occurs in the neural tube.

form neurons and glial cells. After the neuron is formed, the neuron will migrate to its place in the brain which will then grow axons and dendrites from the cell body. The projection neurons will branch out and form connections with other cells, or what is known as a synapse. At the synapse, nerve impulses are carried from one cell to another. Several neurons will then form certain neural pathways that are further matured through programmed connection and elimination processes, depending on stimulation and input from the environment. Important cells and connections will be maintained and developed, while those that are useless will be eliminated. In this process brain plasticity occurs, the brain organizes neurons to adapt to the environment or repair neurons after a brain injury (Prado & Dewey, 2014).

The early postnatal period of human life is an important phase, 80% of brain development and maturation occurs in this period. In the first 24 months, nerve cells (neurons) on the surface of the brain will experience growth, both in number (neurogenesis) and connections (synaptogenesis) between neurons (Grantham-McGregor et al., 2007). Connections between neurons or called synapses will be formed by protrusions from the neuron cell bodies or what are called dendrites and axons. The formation of new synapses is an important component in human cognitive development, which allows the formation of new memories, learning processes, and the formation of skills (Ropper et al., 2014; De Onis & Branca, 2016). In addition, at this time there is also the formation of a fibrous sheath (myelin) which will cover the axon. Previously, this nerve sheath was only thought to play a role in increasing the speed of nerve impulse conduction, but recent studies have shown that myelin also plays a role in cognition, learning, and IQ, through mechanisms of speed regulation and synchronization of impulse conduction between various regions of the brain (Fields, 2008).

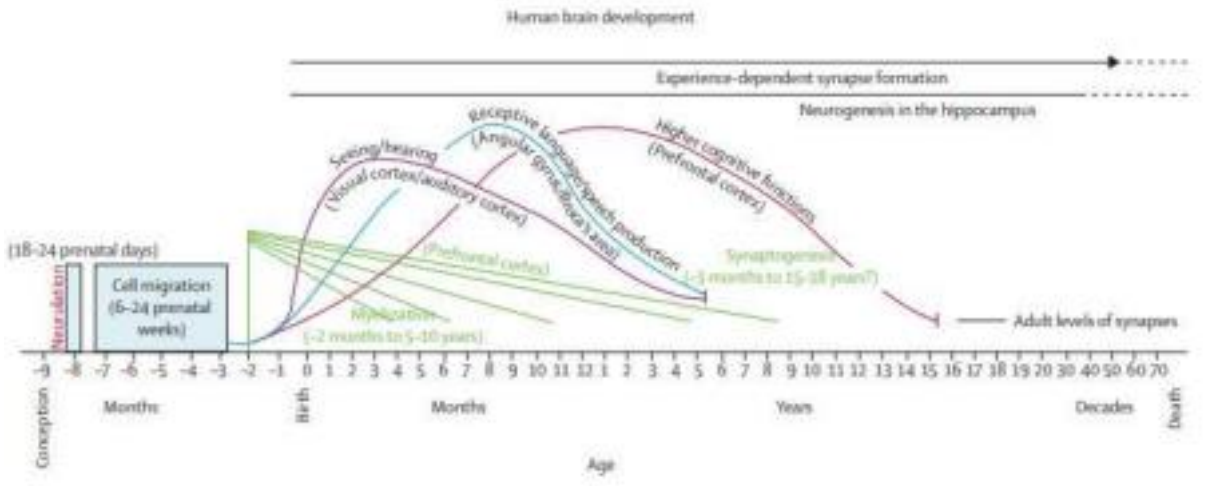

Figure 2. Brain development in children. The most rapid brain development is seen in the first 2 years of life, and includes the development of various cognitive domains, including the maturation of the organs of sight, hearing, language, and higher cortical functions (Grantham-McGregor et al., 2007).

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Disorders Of Brain Development Due To Stunting

Stunting is an indicator of nutritional adequacy in children. Stunting, together with inadequate cognitive stimulation, iodine deficiency, and iron deficiency anemia are major risk factors for impaired brain development. The effect of stunting on brain development mainly occurs in the postnatal period.8Children with stunting have a risk of experiencing deficiencies in macronutrients and micronutrients. Macronutrients include protein, carbohydrates and fat, while micronutrients include vitamins and minerals, such as zinc and vitamin B12. There are four micronutrients that are primarily associated with brain development, namely iodine, zinc, vitamin B12, and iron.

Protein, carbohydrates and fatty acids are macronutrients that are important for brain growth. Protein plays a role in almost all processes of neurodevelopment, from neurogenesis, axon and dendrite growth, synapse formation, myelination, and apoptosis. At autopsy of infants with Intrauterine Growth Restriction (IUGR), patients with protein malnutrition have less cortical gray matter volume compared to normal infants. Dendrite branching and connection complexity are also less, thus affecting the number of synapses which are also less. In experimental animals, nutritional restrictions on Baboon mothers will cause Brain-derived Neurotrophic Factor (BDNF) and Insulin-like Growth Factor-1 (IGF-1) in offspring becomes less, and this can trigger apoptosis (Prado & Dewey, 2014).

Fatty acids play a role in the process of neurogenesis, synapse maturation and myelination. Neurogenesis requires the synthesis of large amounts of phospholipids to form the cell membrane of neurons. Docosahexaenoic acid (DHA) deficiency has been shown to decrease neuronal proliferation. Arachidonic acid and DHA in cell membranes at synapses play a role in synaptic maturation and in neurotransmission processes. In addition, fatty acids are also important components of myelin, and pre and postnatal fatty acid deficiencies can change myelin composition (Prado & Dewey,2014).

Iodine deficiency is associated with impaired thyroid hormone production, namely tiroxine (T4) and triiodotironine (T3). This thyroid hormone has an important role in neurogenesis, neuron migration, synaptogenesis, and myelination. Moderate deficiency is associated with intellectual development delays and interferes with academic functioning, while severe deficiency is associated with intellectual disability. Apart from iodine, another micronutrient that is important for the development of the central nervous system is zinc. Zinc plays a role in neuron formation, neuron migration, and synapse formation. Zinc is found in high concentrations in the hippocampus, cerebellum, prefrontal cortex, and limbic system. Human studies have demonstrated a positive association between prenatal or infant zinc levels and motor development (John et al., 2017).

Vitamin B12 plays a role in DNA methylation, epinephrine synthesis and methionine synthesis. The fetus gets vitamin B12 from the placenta from the mother. After birth, babies mainly get their supply of vitamin B12 from animal food sources. Vitamin B12 deficiency is mainly associated with demyelination, which causes delays in cognitive development. A longitudinal study shows that prenatal vitamin B12 deficiency is associated with impaired cognitive function at school, especially the function of the frontal lobe for perception and performing tiered tasks, and the function of the temporal lobe for short-term memory. Iron deficiency is a global health problem. Iron is mainly related to the synthesis of hemoglobin and has an important role in delivering oxygen to all tissues, especially the brain. Besides that, frontal, and development of the basal ganglia. In children, iron deficiency is associated with impaired

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social-emotional behavior, including shyness, slow response, and anxiety. Iron deficiency anemia in children is also associated with impaired mental and motor development.

There are several mechanisms responsible for impaired brain development in children with stunting, including disturbances in the formation of synapses, defects in myelin formation, and inflammatory processes in the central nervous system.

Impaired Growth of Axons, Dendrites, and Synapse Formation

The process of growth of axons and dendrites begins at gestation and lasts up to 2 years of postnatal life. In children who are stunted, the dendrites of neurons in the cerebral cortex will be fewer, shorter, and have an abnormal shape (figure 3). This abnormal formation of dendrites will cause the formation of synapses to be limited.

The synapse is the connection between the axon, dendrites and the cell body.3Synapses between neurons formed by dendrites are important factors influencing learning, memory, attention, language, skill formation, and visuospatial abilities. Synapse density reaches a maximum at different times between different areas of the brain. The visual cortex reaches its maximum at 4-12 months postnatally, while the prefrontal cortex after 15 months postnatally. The image below shows a comparison between brain tissue in normal children and the brain in children with stunting (De Onis & Branca, 2016).

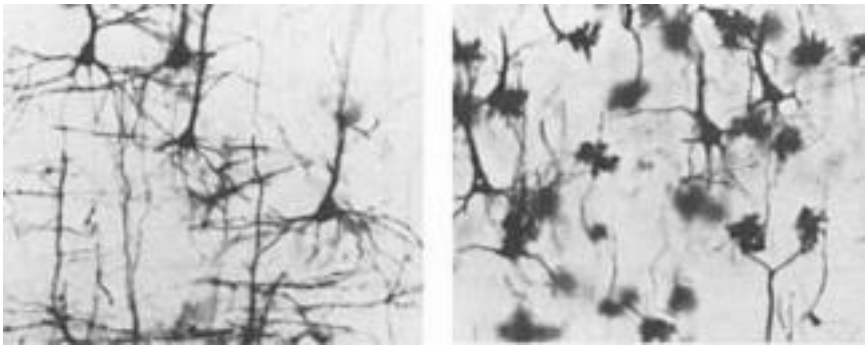

Figure 3. The left image shows neurons in a well-nourished child. The dendrites appear normal and have extensive branches. The right image shows neurons in a stunted child, showing neurons with short dendrites, few branches, and abnormal shape (De Onis & Branca, 2016).

Disorders of the Myelination Process

In addition to disorders of synapse formation, children with stunting are found to have deficiencies of essential amino acids. Essential amino acids are very dependent on intake from the diet because they cannot be produced by the human body. One of the essential amino acids that is deficient is sphingomyelin, the main lipid component of myelin, which plays an important role in the myelination process of the central nervous system.9Disorders of myelin formation will cause a tendency to experience cognitive disorders, especially learning, and information processing, and psychiatric disorders, such as schizophrenia, chronic depression, bipolar, obsessive compulsive disorder, and post-traumatic stress disorder (Fields, 2008).

Neuroinflammation

Children with stunting have a high risk of experiencing infection. There are various infections that can affect children of all ages. Some of the infections that are often found include worm

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infections, diarrhea, and malaria. The infection mainly affects children under 3 years of age (John et al., 2017).

Diarrhea in the first two years of life is associated with cognitive impairment in childhood, according to several studies, especially in Brazil and Bangladesh. Other infections such as intestinal helminthic infections, schistosomiasis and malaria are also known to cause impaired brain development. All of these infections do not directly affect the central nervous system, but play a role through an indirect mechanism that has not been well explained yet, but is thought to be caused by inflammation. Other infections can directly affect the central nervous system, such as HIV infection, bacterial meningitis and viral encephalitis (Semba et al., 2016).

Apart from infection mechanisms, inflammation can affect brain development through non-inflammatory mechanisms. There are several environmental causes, such as exposure to cigarette smoke in children, pollutants, and pesticides which can induce systemic inflammation and cause impaired brain development.

Although the underlying mechanism is unclear, the interaction between nutrition, inflammation, and brain development is thought to be very strong. One of the theories currently being developed that connects these three components is microbiome and environmental enteropathy. Inflammation and malnutrition can cause changes in the microbiome and further changes in the microbiome can affect nutrition and systemic inflammation. Changes in the microbiome can affect brain development and behavior through the “microbiome – brain – gut axis”.

The gut microbiome plays a vital role in microglial maturation and function. Microglial are immunological cells present in the brain. Early in development, microglia actively regulate the number of neuron cells, synapse maturation, and form neuronal circuits. Microglials also play a role in neuroinflammation by monitoring the microenvironment in the brain and facilitating tissue repair and antimicrobial effects, in other words maintaining homeostasis. Microglial dysfunction has been found to play a role in neurodevelopmental diseases and neurodegeneration. Apart from being influenced by cytokines and chemokines in the central nervous system, microglial activity was also found to receive input from the gut microbiome via vagus nerve afferents.

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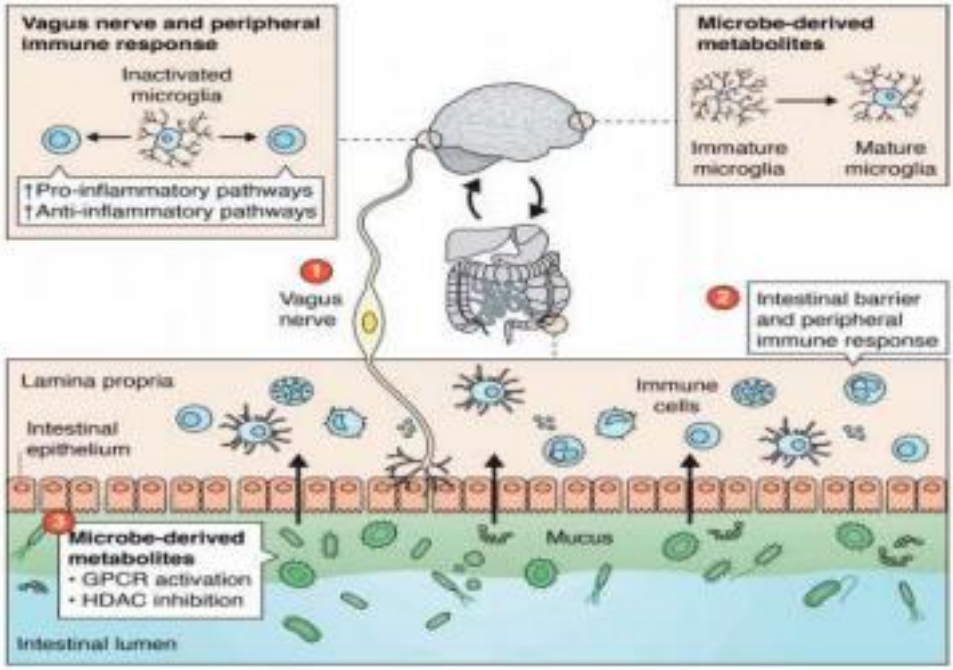

Figure 4: Gut-brain communication pathways. The microbiota in the gut and central nervous system communicate with each other through several pathways. Microglial maturation and function depend on the gut-brain axis connection. Information about peripheral inflammation and the health of the gastrointestinal system is received by the central nervous system via the vagal nerves. This input will influence microglial activation and neuroinflammation. The presence of inflammation in the intestine will affect the inflammatory response in the central nervous system.

Impaired brain development due to stunting mainly occurs in areas of the brain that play a role in cognition, memory and motor skills. In stunted children, disturbances occur in the formation of circuits that play a role in learning and memory in the medial hippocampus, as well as disturbances in the neuron network in the prefrontal cortex which plays a role in executive function (John et al., 2017). Children with stunting have a tendency not to attend school, attend school later, get poor grades at school, and have worse cognitive abilities than normal children. The child's curiosity will also decrease, and the child will appear apathetic. Apart from cognition, children with stunting also tend to be more susceptible to experiencing psychiatric disorders, especially excessive anxiety and depression (Prendergast & Humphrey, 2014).

There are two factors that influence the effect of stunting on brain development disorders, namely the type and degree of nutrient deficiency and the time of deficiency.

Degrees of Nutrition Deficiency

The more severe the malnutrition, the more disrupted brain growth will be. In cases of mild malnutrition, this may be compensated for by some homeostatic mechanism. Some of the mechanisms referred to include the redistribution of cardiac output to vital organs, especially the brain, when nutrition and oxygen are inadequate, increased transfer of iron from the placenta when iron deficiency occurs in the mother, and several other mechanisms. These compensatory mechanisms differ depending on the type of nutritional deficiency with different thresholds.

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2. Timing of Nutritional Deficiencies

Impaired brain development becomes severe, especially when it occurs during a critical growth phase, namely the first two years of life. But this also depends on the type of nutritional deficiency. Developmental disorders will occur if nutritional deficiencies occur in the period when these nutrients are needed by the body. For example, DHA is required for myelination, and myelination of the auditory pathway occurs from 26 weeks of gestation to 1 year, so that in that period DHA supplementation can be considered.

This is important to understand because it has implications for the limited deadline for stunting management. Cohort studies show that improved nutrition in the first 2 years of life will improve children's performance at school, but not if nutritional improvements occur after the age of two (Prendergast & Humphrey, 2014). Other studies have shown that nutritional improvements in children over 2 years of age, up to the age of 11 years, will still improve children's cognitive function, but with a smaller degree of improvement. This relates to the brain's ability to restore after an early disturbance of development. This recovery process occurs in three ways, namely the reorganization of the remaining neural circuits, the formation of new circuits, or the formation of new neurons and glials.3Even though the new concept shows the ability to restore, the possibility of achieving normal cognition will be higher if the intervention is carried out as early as possible, compared to if the intervention is given late. This emphasizes the importance of stunting management as early as possible, with the aim that children's cognitive function in the future will be better, and produce the next generation of quality nation.

Results and Discussion

Stunting Handling Intervention

The application of clinical and basic medical science needs to be designed through comprehensive program implementation efforts to treat and prevent stunting. Primary efforts through promotive actions, secondary efforts with early detection and appropriate management and tertiary efforts with rehabilitative processes need to be integrated across programs and across sectors. This is in line with the national strategy to accelerate stunting prevention through 5 pillars, namely; (1) Commitment and vision of the highest leadership of the State; (2) The national campaign focuses on understanding, behavior change, political commitment and accountability; (3) Convergence, coordination and consolidation of national, regional and community programs; (4) Encouraging the "Nutritional Food Security" policy; (5) Monitoring and evaluation.

To support these five pillars, the stunting management framework is divided into 2 methods: (1) Specific interventions that contribute 30% to the success of treatment, are aimed at children within the First 1,000 Days of Life (HPK), are generally carried out by the health sector and are short term in nature. This can be done through the target group of adolescents and women of childbearing age, pregnant women, nursing mothers and children 0-23 months, children 24-59 months through priority, important and conditional interventions; (2) Sensitive interventions that contribute 70%, are aimed at various development activities outside the health sector with the target being the general public. The types of interventions that can be carried out are increasing the supply of drinking water and sanitation, increasing access and quality of nutrition and health services, increasing awareness, commitment, parenting practices, maternal and child nutrition, increasing access to nutritious food.

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A holistic approach to reducing stunting is carried out through various programs to improve community nutrition, community-based total sanitation, and several other activities through effective interventions by administering blood-boosting tablets (for young women, brides-to-be, and pregnant women), exclusive breastfeeding, MP-ASI, Micro-nutrition supplements (taburia), macro-nutrient supplements (PMT), malnutrition/poor nutrition management, vitamin A supplementation, iodized salt, clean water, sanitation, and hand washing with soap, deworming, and non-cash food assistance. These effective intervention activities will result in adequate nutritional consumption, appropriate parenting styles, increased quality of health services and environmental health which will have a positive effect on young women, pregnant and lactating mothers, as well as two-year-old babies. This comprehensive effort will be successful if it is supported by political will from stakeholders through supporting health and non-health financing, food safety and security, advocacy processes. Therefore, prevention of stunting in brain development disorders requires multi-sectoral support starting with need assessment in identifying community needs by involving specific communities in society in a systematic, structured and organized manner.

Conclusion

Handling the problem of stunting is very important to be addressed immediately. In the context of handling the problem of stunting, various treatment methods can be used.First, specific interventions that contribute 30% to the success of treatment, are aimed at children within the First 1,000 Days of Life (HPK), are generally carried out by the health sector and are short-term in nature. This can be done through the target group of adolescents and women of childbearing age, pregnant women, nursing mothers and children 0-23 months, children 24-59 months through priority, important and conditional interventions. The two sensitive interventions, which contribute 70%, are aimed at various development activities outside the health sector targeting the general public. The types of interventions that can be carried out are increasing the supply of drinking water and sanitation, increasing access to and quality of nutrition and health services, increasing awareness, commitment, parenting practices, maternal and child nutrition, increasing access to nutritious food.

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