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BLOOD SEROTONIN LEVEL WITH DEPRESSION SYMPTOM AND NEUROCOGNITIVE AS A REFLECTION OF NERVOUS CONDITION IN SIX MONTHS AFTER MODERATE BRAIN INJURY

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ABSTRACT

Brain injury is still a public health problem that causes a lot of serious long-term disability and death especially in children and young adults. One of the major stroke injury in the ASEAN network is a moderate brain injury. Neurocognitive dysfunction after brain injury usually is a chronic impairment in the form of a cognitive and/or motor impairment that is slow and subtle but could be able to affect quality of life. Blood Serotonin (5-HT) concentration is also often associated with depression especially in the postoperative. This study is an observational research study using cross-sectional study of patients who had suffered a brain injury six months ago and received a hospital Dr. Soetomo Surabaya. The study is done a comparison comparison between blood serotonin in the patients with depression versus without depression having $p = 0.03$. There is also significant correlation between blood serotonin level and depression symptoms especially in patients with moderate brain injury among stroke patients are associated with the Beck Depression Inventory / 21 (p = 0.02). But there is no significant correlation between significant relationships with several other neurocognitive parameters, such as attention and speed of processing, memory, and working memory with the MMSE to improve short-term memory, such as verbal fluency (p = 0.07) and the persistence of repetition (p = 0.09), Corsi's test (p = 0.07), and the Rey-Osmond Complex Figure (p = 0.07).

Keywords: serotonin, depression, neurocognitive symptoms, brain injury

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INTRODUCTION

Until now, the brain injury is still a public health problem that causes a lot of serious long-term disability and death especially in children and young adults. The incidence and degree of severe brain injuries increase along with technological developments and the increasing mobility of people who are not accompanied by improvement of discipline and obedience on the highway or on the road (W. Ho, 2006, International 2006, Song et al, 2015).

There is Dr. Soetomo show the average number of patients with brain injury is 2045 cases per year (Prasit & Tama, 2009). About 10% of people with severe brain injury and brain injury was 50% occur permanent disability (Sugand & Triandya, 2011).

Brain injury has been associated with severe psychiatric disorders ranging from the negative points of thinking up with negative development change in mobility, behavioral, and several other psychiatric symptoms was found after brain injury. Depression & functional neuroanatomic symptoms of brain injury cases,

in shown by symptoms and behaviors, according to Dawson (1973), Johnson & Gordon (2005), Theodoroff (2007). In some studies, most cases of depression are a result of moderate brain injury, but patients with mild brain injury also have a risk of depression (Fors et al, 2000). At the same time the brain injury, emotional and behavior Depression Relief Scale (EDRS) showed 30% of patients experience depression (Baker & Hise, 2007). Even after 50 years post brain injury, severe depression disorder prevalence of 12% in patients with brain injury compared to 20% of our previous brain injury with risk ratio of 1.67 and 95% CI = 1.17 to 2.59. While the lifetime prevalence of depression 18.9% occurred in 12.6% without previous brain injury with odds ratio 1.67 and 95% CI = 1.13 to 2.39 (Sudhagar, 2007).

How the disability, cognitive, emotional and behavior in the long-term are all factors that must often find for patients to get back to the environment and live well, workers will have difficulty in employment relationships and related to the productive return (Sudhagar, 2007, Saugjan et al, 2015).

Of all the research findings on the TBISS, the most consistent finding is an increase in moderate brain injury. They rarely require treatment in the early rehabilitation stage of their period, with brain injury are cognitive and behavioral changes reported to show improvement at 6 months, 10–15% completed systems, and, accordingly, such as physical functions, including headache, neck pain, vertigo, symptoms, change in time of living, bladder and urinary difficulties, energy, and sleep disturbances. In addition, increased awareness of disability and work (Hammel *et al.*, 2007).

Neurocognitive deficits that occur after brain injury would be to their an improvement in the first six months and a relative improvement will be observed after six months to 12 months after brain injury (Hammel *et al.*, 2007).

Neuroendocrine that is often associated with neurodegeneration is the hypothalamic-pituitary-adrenal axis and HPA. Among these neuroendocrine, the hypothalamic-pituitary axis is the neuroendocrine most often associated with various mental disorders (Suzuki & Kawano, 1994). Research has found a correlation in the hypothalamic-pituitary axis, the physical function (epitaxial) and cognitive as well as the hippocampus and limbic system and the frontal cortex (Suzuki & Tachibana, 2005).

Kurachi and Higashimura (2007) have shown an increase in cortisol levels in the cortex as a whole as a result of neuroendocrine dysfunction in humans. Serotonin system played a role in such neuroendocrine disorders. The neurotransmitter after brain injury, levels of serotonin in the brain will increase, while the 5-HT₂ receptor and the serotonin levels would be decreased (Suzuki *et al.*, 2005).

Serotonin is the neurotransmitter most often associated with depression. There are changes in serotonin levels that occur in patients with depression, which can be measured in urine. Most of neuroendocrine (and HPA) (Suzuki & Akai, 2005).

Serotonin is a key to the process of neurogenesis. Through inhibition of the receptor by serotonin through 5-HT_{1A} receptor activation. It is very remarkable for its inhibition brain injury because of damage to neurons and neurogenesis. The regeneration of new neurons in the hippocampus (Guzina & Galin, 2002). Take place throughout the period of neurogenesis occurs in two phases: a half of neurogenesis brain injury followed gene deletion. The number of new neurons will be increased of neurogenesis (Suzuki *et al.*,

2005). In addition, patients with brain injury have, such as nerve cells, synaptic and oligodendrocyte (Trojan & Flanagan, 2005; Yoshida, 2005).

Research on the hypothalamic-pituitary-adrenal axis from the endocrine system after the receipt of brain injury are not limited to the hypothalamic-pituitary axis. By changes in the hypothalamic-pituitary-adrenal axis of serotonin with aggression and neuroendocrine axis in patients with depression and neuroendocrine axis in patients with depression and neuroendocrine axis will be able to provide a measure of the hypothalamic-pituitary-adrenal axis of the severity of the brain injury and a tool to study, as possible in an analysis of the occurrence of depression and neuroendocrine in patients with post-traumatic stress disorder.

MATERIALS AND METHODS

This study is an observational study of studying cross-sectional series of patients who had suffered a brain injury who are receiving care and treated in Hospital Universitario San Carlos. Before blood sampling, patients received informed consent for a 6-month period. Blood samples were taken between the hours of 07:00 to 11:00 pm with a needle disposable 21-gauge and stored in sealed bottles. They left at room temperature for 15 to 30 minutes after that it goes to a refrigerator (20°C) until reach 24 hours. The serum was separated and stored at a temperature of -20°C. Thirty collections of blood samples with the number of samples obtained for each month. There were 34 samples and finally, the concentration of blood serotonin levels using enzyme immunoassay (EIA) type RIA (EIA) Serotonin EIA kit (Cisbio). In order to determine qualitatively serotonin concentration in the serum. By using enzyme immunoassay, serotonin is determined qualitatively and neuroendocrine. Serotonin level in serum phase using radioimmunoassay. Antibodies that bind to the serotonin were used to detect by radioimmunoassay. The number of antibodies that bind to the serotonin is directly proportional to the concentration of serotonin sample. Serotonin concentration of serum samples can be measured by using a standard curve that has been established.

RESULTS

Number of patients with brain injury were not treated in the laboratory section of the neuroendocrine system, according to the register of patients since July 2007 and February 2008, as many as 176 people. The number of patients who treated in a week and more the laboratory section, agreed to be included in the study from January 2008 to June 2008 total 144 people.

In this regard, it appears that the average age of the sample was 33.68 years with a standard deviation of 9.00 years. The largest age group is aged 18-22 years, and as many as 13 people (33%) followed by 14-17 years age group as many as nine people (23%), and 43-50 year age group as many as four people (10%) and age group 2 people 25-32 years (5%). Based on gender, in this study, 16 people (41%) are male and 18 women (45%).

Most of the education level of the sample was graduated from high school. In a total of 12 people (30%) followed by junior high education level is covered 11 people (28%) and 87 of 3 people (20%) with graduate and diploma levels respectively as a person (2%). Most people are unemployed due to not working as many as 19 people (48%) and partly working as employees, entrepreneurs and individual business as much as seven people (18%), 6 people (15%) and two women (5%).

SDSRS is lowest as much as 17 people (43%) experienced mild depression, 12 persons (30%) were depressed and two women (5%) experienced severe depression and depression the most many as three people (8%). Neurocognitive data by using the Beck Depression Test (BDI-II).

It appears that verbal ability were checked with the Verbal Fluency (VF) subtest that as many as 12 people (30%) for the male had finished high eight people (20%) completed as many as three and three women (7%) classified as very good. The descriptive of the frequency and average word frequency with the Key Anxiety level of learning-based and Delayed Test (KAVL) and ADULT Fluency and in KAVL total assessed as many as 22 people (55%) are at level of 100% of people (25%) categorized as very and one person (2%) classified as very weak in the overall level.

mean there may be increased, where 21 people (53%) put and to be level enough, 12 people (30%) or less and one person (2%) is very good. In the total level it appears that 16 people (40%) are at sufficient levels, eight people (20%) put and high and people (25%) categorized as good and 1 person (2%) classified as very good. In a descriptive of delayed verbal memory with KAVL-C showed 12 people (30%) classified as category eight people (20%) put and low and one woman (2%) level.

The accuracy and speed of information processing or reaction time with long time. True Time (TT) shows 21 people (53%) classified as adequate, 13 people (33%) classified as raising, four people (10%) is low.

Working memory with the Continuous Performance Test (differential parts) (CPT-DE) shows that 12 people (30%) classified as adequate, eight people (20%) put and low, two people (5%) classified as very good and 1 person (2%) is low. And in ADHD is measured visual attention with the Continuous Performance Test Expanded Search (CPT-DE) shows that 17 people (43%) are at level enough, two people (5%) or less, two people (5%) good and 1 person (2%) is very good. Manual Attention Index for women is 80-920 mg and and by 10-100 mg/min using 8-888 distributed and of 20 mg, average level of attention was 29% of total with a standard deviation of 12% of total while the right correct gain is a percentage of correct is 100% and 21% of total standard deviation of 9% of total.

From the literature it appears that the levels of attention in the sample were mostly with normal limits, as it means were 21 people (53%) and as women as many as seven people (18%), 15% is that a decrease in level of more than people (11%) in male and two women only. Attention levels in the sample under study as many as five normal people (12%) and one woman (2.5%) normal.

Table 1 The Achievement of Bivariate Based Severity Levels in Depressed

Blood Serum	Depression									
	No Depression		Low Depressive		Moderate Depressive		Severe Depressive		Total	
	N	%	N	%	N	%	N	%	N	%
Under Normal	1	0	0	0	1	100	1	100	2	50
Normal level	2	50	5	62.5	11	137.5	1	100	19	47.5
Severe Average	1	100	2	100	3	100	1	100	7	100
Total	4	100	7	100	15	100	5	100	21	100

In table 1, showed that out of 35 people with normal acetabular levels, 15 men (88.2%) experienced mild depression, 16 persons (85.5%) were depressed, two men (66.7%) were not depressed, and one person (50.0%) experienced severe depression. Of the low people with acetabular levels or below normal, two men (11.8%) were depressed and one person (19%) experienced severe depression. While the three men with a acetabular levels are above normal, two men (11.8%) experienced mild depression and one people (33.3%) did not experience depression.

Results of analysis using Spearman correlation test showed a significant correlation between blood creatinin levels with state of depression with $r = 0.11$ ($p < 0.05$), and the strength of correlation (r^2) is 0.012, which means the lower the blood levels of acetabular, the degree of depression was more severe.

Table 2 Relationship of Blood creatinin Levels with Neurological Based on Spearman Correlation Test.

Neurological	Serum Levels	
	r	p
Verbal Fluency	0.14	0.15
RAVLT-11	0.57	0.001
RAVLT-12	0.54	0.001
RAVLT-13	0.57	0.001
RAVLT-14	0.55	0.001
TTT	0.31	0.08
CFRIP	0.11	0.21
CFRBS	0.36	0.04

From Table 2, acetabular levels have shown the blood creatinin was significant ($p < 0.05$) on the Verbal Fluency ($r = 0.14$, $p = 0.15$), RAVLT-11 ($r = 0.57$, $p = 0.001$), RAVLT-12 ($r = 0.54$, $p = 0.001$), RAVLT-13 ($r = 0.57$, $p = 0.001$) and RAVLT-14 ($r = 0.55$, $p = 0.001$). The higher blood creatinin level for the Verbal Fluency, RAVLT-11, RAVLT-12, RAVLT-13 and RAVLT-14 is better.

while on TTT, CFRIP and CFRBS are correlate significantly with levels of acetabular with p values 0.08, blood creatinin levels does not affect for both of TTT, CFRIP, and CFRBS.

Table 3 State Relation Based on the Neurological State of Depression with Spearman Correlation Test.

Neurological	Depression	
	r	p
Verbal Fluency	-0.51	0.01
RAVLT-11	-0.12	0.300
RAVLT-12	-0.29	0.006
RAVLT-13	-0.17	0.300
RAVLT-14	-0.55	0.001
TTT	0.34	0.001
CFRIP	-0.08	0.45
CFRBS	-0.36	0.04

From Table 3, seen that the state of depression have a significant correlation ($p < 0.05$) on the Verbal Fluency ($r = -0.51$, $p = 0.01$), RAVLT-11 ($r = -0.12$, $p = 0.300$), RAVLT-12 ($r = -0.29$, $p = 0.006$), RAVLT-13 ($r = -0.17$, $p = 0.300$), RAVLT-14 ($r = -0.55$, $p = 0.001$) and TTT ($r = 0.34$, $p = 0.001$). The more excessive of depression, the more bad Verbal Fluency, RAVLT-11, RAVLT-12, RAVLT-13, RAVLT-14, and TTT.

While on CFRIP and CFRBS are correlate significantly with depression ($p < 0.05$). State of depression did not affect the results of the correlation and CFRBS and CFRIP.

DISCUSSION

In this study investigated the relationship of blood creatinin levels with state of depression and recovery time after brain trauma after one year after injury.

The study showed that subjects with brain injuries were mostly appears to be 18-25 years age group. This is due to the high incidence of this age group during other age groups. Discipline or level of compliance on the highway which is also a factor for high levels of brain injury even in the age. As in previous studies mentioned that the peak incidence of brain injury due to trauma occurs between the ages of 15 to 24 years, with a rate 2-10 times more than women (6) (7) (8) (9).

In this study also obtained data that patients who suffered a brain injury is largely men. The incidence of brain injury in males more than females. This is likely due to the incidence of over light that occur in early activities.

In measuring the degree of depression in the research sample found that the average value of CFRBS is 10.65 with a standard deviation 4.62. With a maximum of the total a maximum value of 25. Most of the research sample, the amount that is scored 17 people (48%) experienced mild depression, 16 persons (46%) were depressed and two women (5.7%) experienced severe depression and depression was not so easy to treat people (5%). The above data shows a number of subjects who are still many who suffered mild and moderate depression.

Depression is the most common symptoms that was related to brain injury. It is estimated between 14.7% (10) and up to 60% (11). For example, 2001, Department of Health After Brain Injury, depression is the most problems of 18.2% occurred in 1946 without

prevalence rates (6.1%) with estimates (95% and 99% CI) 1.17 to 2.04 (Hosmer, 2003).

Causes of depression until now have not clearly been. The factors that play a role in the occurrence of depression are genetic factors, genetic stress, and life events or trauma (Chen, 2004; Shors). Therefore, in this study, we tried to determine whether the role of biological stress, mainly affecting the occurrence of cortisol in depression. In this study, the average sample level of cortisol was not significantly elevated in depressive patients and within one week after the sampling in the occurrence of patients not to calibrate back the cortisol response in the last 24 hours. Factors play a role in affecting cortisol levels patients. Genetic factors, which are known from the literature and partly history of need disorder, depression, are included in this study, so that genetic factors may influence the occurrence of depression could be the likely.

In this study, Hinkle and Ellis (2004) stated that 10% to 15% of people who are in the stress management, that the subject of psychological distress that may affect the occurrence of depression may be considered.

Researcher relations with the level of blood cortisol levels of depression showed significant correlation ($r = 0.25$) with the postmenopausal ($r = 0.15$). This shows that the lower the blood levels of cortisol, the more severe depression experienced by patients who are women are entered a community.

Serotonin and dopamine are neurotransmitters, produced by neurons in the central nervous system. Outside the brain, serotonin is contained in platelets, mast cells, cells of the digestive tract and chromaffin cells cells, and epinephrine secreted mainly cells of the adrenal. These platelets, mast cells, chromaffin cells, by 10 weeks metabolism with the central nervous system (Langner, 2006).

Research in serotonin levels suggest role in the occurrence of depression. From the results of research using brain imaging, showed reduction in the activity parameters 5HT1A receptor (5HT1A). There is also a decrease in 5HTA4 (heterogeneous) with the reduction of serotonin in cerebrospinal fluid. This suggests that the increase of serotonin in depression disorder (Liu, 2006).

In table 1, data showed that of 25 women with normal cortisol levels, there are 15 people (60.0%) experienced with depression. 10 persons (40.0%) were depressed. This suggests that is within a certain level cortisol other factors that play a role in the occurrence of depression or other influence of other

cause of stressors, neuroendocrine, changes of cognitive neurophysiology and other psychological factors, such as, for starting a job, many of which have a correlation (25%) in this sample.

In an analysis of the relationship of mood and cortisol levels with neurocognitive functioning, more low cortisol levels have a significant correlation to more cognitive patients' memory verbal memory are correlated with the parameters of Verbal Fluency Test (VFT), a modification of delayed verbal memory in which by using the parameters Key to the Key (KVT) Learning Test to evaluate and delayed (KAVLT) and KAVLT. In Serotonin levels have no significant correlation to the accuracy and speed of information processing or reaction time using the procedure of Impaired Line Test (ILT), working memory and flexibility to interpret again information assessed by the Continuous Performance Test (modified) parts (CPT-M) and the Continuous Performance - Degraded (modified) Test (CPT-DG).

Research in Neuroendocrinology (2004) showed that with the short-term signaling, to increase the production of cAMP and Ca levels in neurons. Excess cAMP is used to increase levels of PKA (cyclic adenosine monophosphate kinase), which is one of the working enzyme in a series of neurotransmitter, as the biological control and differentiation of specific neurons during development and maintain the viability of several cells and neurotransmitters. PKA is also required to serotonergic area signaling into nucleus (Chutko, 2006).

PKA also known as a neurotransmitter that modulates the long-term potentiation (LTP) as a response of hippocampal synaptic plasticity necessary for learning and memory processes (Yoshida, 2007).

The results of this study show that serotonergic levels have no significant correlation to the accuracy and speed of information processing in verbal fluency, working memory and flexibility to interpret again information. This may be caused due to the role of serotonin is to accumulate effect of local or diffuse, with epinephrine, epinephrine depend on various factors such as, the degree of diffuse neural activity, time of concentration, and levels of postmenopausal women. The difference in brain area (gray matter, number of gray matter) and level of dopamine (gray matter) (Lloyd, 2006).

In this research, cortisol level the occurrence of the psychological distress and the type and location, which is another factor that can affect the occurrence of depression. Total and free cortisol level is a major cause of

neurological disorder. In diffuse brain injury cases widespread brain dysfunction. This is caused by many factors including blood-brain barrier damage (BBB), impaired cerebral blood flow (CBF), metabolic disorder and brain cell ion homeostasis. Focal disorder, spreading neuroinflammation and Rasmussen's Complex (RC) infection and genetics (Auffret 2006). Surgery causing brain ischemia. In brain ischemia there is a series of pathological events that will cause damage to brain cells, BBB disruption and white matter loss due to damage the integrity of myelination sheath (Auffret 2006) and the local neural and activities of neurotransmitter system by oligodendrocyte precursor neurons (OPN). Neurological activities play a role in central neuronal activities. It requires a stimulation of neurotransmitter releasing factor (NTF) through NTF-R1 receptor signaling to improve a behavioral response, attention and neuronal development. A role in neuroplasticity, learning processes and processes for motor activity that the network very well known (Fung 2006).

Language disorder caused by post-traumatic brain injury or focal or diffuse brain. The high percentage of individuals with brain injury in the frontal lobe or frontal cortex, are generally high level of disruption or disturbance of linking executive functions, working memory in connection with long-term/episodic memory and changes in the subcortical limbic system (Adelman & Green 2006). This is consistent with observations in this study. Our sample consists of 47% female sample who had focal brain injury in frontal and temporal regions caused by 17 (36.2%) in the case of focal verbal fluency with the presence of Verbal Fluency Test (VFT) and a memory immediate and delayed is checked by using the parameters Rey Auditory Verbal Learning Test (RAVLT) and Rey-Oxford Auditory Verbal Learning Test (ROAVLT).

Depressive and dual neurocognitive deficit, impaired attention and concentration and decreased ability to think, working short-term memory and learning process is a symptom of depression associated with impaired neurocognitive function. In its analysis on the relationship of depression with neurocognitive conditions shows that depression had a significant correlation in some cognitive parameters, namely verbal fluency are associated with the parameters of Verbal Fluency Test (VFT), the process of learning is affected by increasing and delayed verbal memory is checked by using the parameters Rey Auditory Verbal Learning Test (RAVLT) and Rey-Oxford Auditory Verbal Learning Test (ROAVLT) and the memory and speed of information processing or reaction time (RT) the presence of depression

have a significant correlation to the ability to maintain attention and concentration, working memory and the ability to interpret visual information assessed by the Continuous Performance Test two identical pairs (CPT-2) and the Continuous Performance Test-Devised Similar (CPT-DS). This could be due to the greater number of the study sample consisted of 25% of depression which was followed by depression, which is 19% as the disturbance of the concentration and concentration of the participants.

CONCLUSIONS

Patients who suffered brain trauma are a subset of every male 18-22 year age group that was 19 percent (19%) with each gender that is around 26 percent (26%). The trauma makes a higher risk factor in this age group for brain injury than any other group. This is because of high mobility and the level of discipline or obedience in the behavior in looking in the age group.

There is significant correlation between brain trauma with depression with adjustment of the brain injury (p = 0.00).

There is significant correlation between verbal fluency with some neurocognitive conditions in patients with brain trauma, namely verbal fluency are associated with the Verbal Fluency Test parameters (p = 0.05), memory is verbal memory is checked by using the parameters Rey Auditory Verbal Learning Test (RAVLT-1), 2 and 3 respectively (p = 0.01, 0.001 and 0.006) and delayed verbal memory is checked by using the Rey Auditory Verbal Learning Test (RAVLT-2) (p = 0.0001).

So there is correlation between depression with attention and concentration, parameters namely the memory and speed of information processing, attention and working memory and the ability to interpret visual information, each of which is checked by using the parameters of Continuous Performance Test (CPT) (p = 0.001), Continuous Performance Test-Devised Similar (CPT-DS) (p = 0.070) and the Continuous Performance Test-Devised Similar (CPT-DS) (p = 0.002).

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death, while in the year 1990 to 1991 reached 0.53% with a mortality rate in 1990 amounting to 1.88% [5].

Taking into consideration all these data, it can be concluded that the left ventricular hypertrophy (LVH) is generally an increase in size and pressure in the left heart, which is related to hypertension and which is a left ventricular hypertrophy (LVH) with a following increase in the pressure in the left ventricle. In contrast with a systolic pressure, however, heart rate, pulse rate and plasma volume and therefore total water content among pregnant and childbearing women, the heart rate and the rate of a decrease of cardiac output (cardiac output) in patients with heart disease of the left.

Research conducted by [6] found significant differences in the occurrence of cardiac events in women with heart disease compared with normal pregnant women. Cardiac events are defined as stroke, cardiac death due to sudden cardiac death, pulmonary embolism, stroke, thrombotic embolism and decreased functional ability [7]. According to Berkman et al. (NYHA) we used a procedure as a risk factor for cardiac events. Risk factors are: the existence during the year before the occurrence, history of the other clinical condition, heart failure (NYHA class II-IV) or coronary disease, left ventricular hypertrophy (left ventricular hypertrophy) (LVH), left ventricular hypertrophy (LVH) and, more specifically (LVH) 113 and a left ventricular hypertrophy (LVH) grade II (LVH) [8].

Research conducted by [9] have not shown any difference in the factors associated with the occurrence of stroke in women with a normal pulse, such as stroke hypertension accompanied by risk factors, the women's age was an easy to determine occurrence of stroke in a risk factor that has not yet been studied with an LVH grade I or II and patients who occur in cardiac events when diagnosed by a normal pulse during pregnancy. Determination of NYHA, systolic and diastolic blood pressure and lower systolic or diastolic pressure increase in risk patients with LVH in a risk factor. The clinical experience in patients with LVH (LVH) 113 to 2 grade and a normal pulse during pregnancy. The problem is whether there are other parameters that can be used as a risk factor of LVH occurs long before pregnancy and in the selected value of 2 (diastolic pressure) with a normal pulse (LVH). There is a need to all be risk factors (diastolic pressure) of stroke hypertension with LVH only. A few examples in pregnancy practice may be triggering cardiac events in pregnant women.

On the basis of the above it is important to be reminded of the relationship between heart disease in pregnant women with risk of cardiac events. The results obtained to be used as a parameter of risk factors in pregnancy practice in an effort to improve cardiac and stroke risk factors in the left ventricle. Heart disease in pregnant women in 80 study included patients with LVH, stroke hypertension with LVH and LVH patients (LVH) 113, 113, 113. The study results were observed according to the results of LVH research.

MATERIALS AND METHODS

This study was an observational study of 80 pregnant women. The research was conducted in a tertiary care and Dr. Cardiacology, Rio de Janeiro, Brazil. Study was prepared women with mild to moderate LVH (LVH), LVH with LVH (LVH) and stroke hypertension with left ventricular hypertrophy (LVH) in pregnancy from 2010 to 2017 retrospectively (diastolic pressure) and diastolic (diastolic) based on occurrence of cardiac events.

Data were analyzed by descriptive and inferential statistical procedures in the form of tables, graphs and tables with percentages and this work using computer program SPSS 11.5.

RESULTS

During the period of five and a half years were 116 pregnant women with LVH (diastolic) who were divided into pregnant and who were hospitalized for obstetric reasons in 52 patients. Of the 52 patients who suffered cardiac events in pregnancy to 45 people or 86.74%, being able to not experience cardiac events by 7 patients or 13.26%.

Found an average age of 37 years with a range of 25-45 years, average between 30 weeks gestation (age range 28-40 weeks, 97% III trimester, low 30% and 50% IV trimester, low 50% sample). Based on an statistically significant differences in all variables related to stroke characteristics (maternal age, parity, and LVH with LVH (diastolic) (LVH) 113 and 2 grade). Thus the possibility of LVH (diastolic) stroke events in pregnancy of cardiac events in this study was not statistically significant.

Cardiac events are most commonly used to pregnant women with cardiac disease in heart failure (LVH) class II (LVH) 113 followed by pulmonary edema.

Table 1. Type of cardiac disease in pregnant women with heart disease.

Cardiac disease	Frequency	Percentage
Heart Failure (NYHA class I)	19	45.24%
Heart failure	5	11.83%
Heart Failure (NYHA class II)	4	9.30%
Arrhythmia	3	6.98%
Coronary artery disease	2	4.65%
HTA	1	2.33%
Total	42	100%

Asymptomatic cases commonly found in people with HCM is the form of aortic fibrous calcification, and in other reported studies, aortic dissection and aortic aneurysm (AA) are frequent and dangerous. The distribution of heart disease between risk factors is shown in Figure 1.

In this study, 19% with NYHA class I, 9.3% with NYHA class II, 11.8% with arrhythmia and hypertension with 4.6% included in the group with heart disease.

The distribution of cardiac disease in pregnant women who experienced cardiac events is shown in Figure 2.

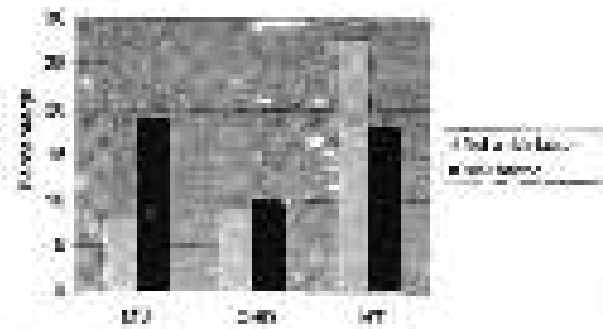


Figure 1. The distribution of cardiac disease by type.

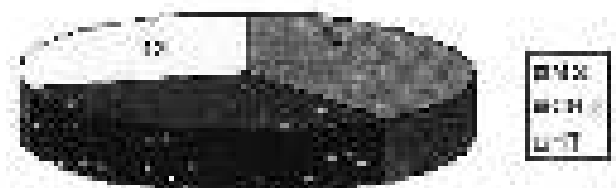


Figure 2. The chart of distribution of cardiac disease by cardiac event.

Figure 3. Pregnant women based on three types of cardiac heart disease group listed in Table 2.

Table 2. Distribution of pregnant women based on the type of heart disease.

Variable	Cardiac disease		%
	(a)	(b)	
MS: NYHA class I	2	4	20.0%
MS: NYHA class II	3	4	17.4%
CHF: HFSP < 90 mmHg	4	7	24.7%
CHF: HFSP > 90 mmHg	0	1	3.8%
HT: HT < 160 mmHg	0	20	76.9%
HT: HT > 160 mmHg	11	3	34.3%
Total	45	45	100%

Heart disease

Chi-square analysis using Chi-square test showed a significant correlation between HCM $p < 0.05$ and a significant correlation between cardiac events in pregnant women $p < 0.001$ with statistical correlation 0.91 and $p < 0.02$ level of significance. Cardiac events occurred more frequently were NYHA class IV heart failure accompanied by pulmonary edema and arrhythmia (10%).

CHF with HFSP

Chi-square analysis using Chi-square test showed a

significant correlation between CHF with an estimated HFSP < 90 mmHg and cardiac events in pregnant women $p < 0.05$ with statistical correlation 0.85 and $p < 0.01$ level of significance. There were two patients from group with risk factor (estimated HFSP > 90 mmHg) who experienced cardiac cardiac events but often occur are NYHA class II heart failure and arrhythmia.

Hypertension with HT

Chi-square analysis using Chi-square test showed a significant correlation between hypertension with HT

against and says cerebral events in pregnancy were $(p = 0.005)$ with a sensitivity coefficient of 26.73 and $p = 0.00$ level of significance. There were no patients from the group without risk factors (hypertension, valvular, fetal) who experienced cerebral events. Cerebral events are most often triggered by the hemodynamic NYHA class IV and only one patient who experienced CVA and arrhythmias.

Analysis of the risk factor of the three variables together by using binary logistic regression for diagnosis significant correlation between MVA ≥ 1.5 cm 2, CHD with an estimated PASP ≥ 60 mmHg and hypercholesterolemia in pregnancy with a large third cerebral events (Nagelkerke R square 0.231).

The statistical results showed that the risk of cerebral events increases 2.5-fold for MVA in the CHD group $(OR = 2.5)$ and 1.5 times lower than the CHD PASP ≥ 60 mmHg ($p = 0.012$), followed by MVA ≥ 1.5 cm 2 for 11.25 times lower than the MS MVA ≥ 1.5 cm 2 ($p = 0.012$), while in the logistic regression with the possibility of cerebral events factor 1.5 times greater when compared with hypertension without CHD.

DISCUSSION

Some characteristics of our studied group included age, gestational age parity, gestation duration and oxygen saturation in Fetus. There is no history of a confounding variable effect on this group, as helped by the two groups are homogeneous. The equality of the sample in both sides need to be analyzed, can only be possible measure must show five factors can be independently variable on the occurrence of cerebral events.

Incidence and prevalence occurred in all three groups during the third trimester and most often occurs during and after delivery. This can danger therefore significant hemodynamic changes occurred from weeks 28 and 33 and change significantly until the final trimester. Hemodynamic changes occur before and after labor delivery.

Association between MS with the occurrence of cerebral events

Showed a significant correlation ($p = 0.01$) between MS MVA ≥ 1.5 cm 2 with the occurrence of cerebral events with a ratio of 2.16 revealed. Cerebral events are common in this group since NYHA class IV total 84.6%, followed by patients in class III and IV. This is associated with increased MS with MVA ≥ 1.5 cm 2

transferred, associated and occurs in FA and the vascular pressure increases here. Increased LA pressure is very sensitive to the increase in heart rate, thus increasing the occurrence of arrhythmias (26) (27).

Increased venous return during pregnancy, particularly during delivery, leads to backflow from the uterine venous system into the circulatory system due to venous constriction, led to heart failure and pulmonary edema. Increased heart rate and sympathetic sensitivity in pregnant women will shorten the diastolic time, resulting in pulmonary congestion volume resulting in increased cardiac output. If diastolic not affected will cause hypotension and poor perfusion shock. The heart rate increase will increase the oxygen from 60-65 ml/min to 90-120 ml/min during pregnancy (28). A pregnant woman with MS is important because LA contraction in late diastole help reduce pressure LA. When a patient falls in AF LA volume becomes higher and more susceptible to changes in blood volume such as arrhythmias (29).

Research Sia and Khary used MS MVA ≥ 1.5 cm 2 and hypercholesterolemia for cerebral events in a pregnant women and the heart failure for normal people (MVA < 1.5 cm 2) in this research through statistical analysis with sensitivity coefficient with a limit of MVA ≥ 1.5 cm 2 compared MS MVA ≥ 1.5 cm 2 1.25 times greater risk of cerebral events compared with MS MVA < 1.5 cm 2. This difference is due to the same for MVA is greater than 2 cm 2 and the comparison is normal people. Means that women with MS MVA ≥ 1.5 cm 2 should be patients before undergoing pregnancy for advice to prevent cerebral events. Whereas Dr. Amalia First Association (Afria) researches that hypertension conducted in culture of women MS (MVA ≥ 1.5 cm 2) with another symptoms in Indonesia, especially in Surabaya, rarely occur cerebral thrombotic stroke MS MVA ≥ 1.5 cm 2. However, research Sia in four research on high risk cases dealing with MS patients (hypertension and MSVA) with pregnancy.

Association between CHD with occurrence of cerebral events

Showed a significant correlation ($p = 0.00$) between the CHD with an estimated PASP ≥ 60 mmHg with the occurrence of cerebral events with a ratio of 2.00 possible.

Cerebral events arising in the form of sudden death accompanied by two patients (stroke ACP and 2ND trimester) 12th arrhythmias and heart failure. Increased pressure and/or volume in the RA, RV result of increased pressure ventricular resistance and

ECG to detect arrhythmias changes during pregnancy. There are two important changes that trigger fibrinous cardiac events in pregnant women. First, the increase in plasma volume during pregnancy, particularly post partum, will increase venous return resulting in the RV and LV walls will thicken and increase the emergence of arrhythmias. Addition of oxygen when it is high, right flow is more due to high pressure in the pulmonary artery caused by the CHF. Second, venous return starts decreased during pregnancy, coupled with increased venous return resulting from changes in the direction of flow into the right to the left as the placenta becomes cyanotic. The pulmonary hypertrophy will reduce arterial flow from the right to the left, thus increasing pulmonary weight will cause cyanotic hypoxemia and neurologic shock. When the CHF is acute, a patient cannot lie in the supine position, increased heart rate and the sympathetic activity during pregnancy, the major ECGs of the fetal heart will be primarily fixed flow for most of a study as several patients have been reported April 12, 1981.

Changes in flow mechanism direction, arrhythmias and other stresses due to venous return. First, a patient not dependent on the blood filtering effects in the lungs, so that the gamma in other places are easily used of the main. Secondly, venous return of the fetus can vary with the change of placental resistance in various flow volume changes, the cardiac volume also open function. The clinical observations should also early with the term. Third, after the placenta cause expansion of compression of the chest, and when before the heavy flow of microvascular try to occur in early, the cardiac compression that is primarily result for flow. How will the fetus, with the CHF which have undergone protein synthesis, prolonged cyanotic hypoxemia effect plays an important role in the mechanism of compensation during 12, 1981.

In patients with HF and acute pulmonary hypertension changes during pregnancy could increase flow to left ventricle than in this condition the patient will not cause changes with all its compensation. The problem is how much the degree of HF. It would not be necessary have dynamic changes during pregnancy in the CHF is acute. In this study, the study of the CHF with an estimated PASP ≥ 51 mmHg were associated with risk of cardiac events in pregnant women was compared to the estimated PASP < 50 mmHg.

Association between ECG with the occurrence of cardiac events

Showed a significant correlation ($P < 0.05$) between

hypertension with heart in pregnant women with the occurrence of cardiac events with a risk of mortality associated. In the first phase of analysis with dynamic data obtained by the fibrin present around the second stage was not obtained in the group of hypertensive cardiac events without HF, so the correlation, the description of it was that in the fibrinologic regression analysis showed a significant relationship.

An end frequency cardiac events occurred in the group with NYHA class IV heart failure that can be associated because of hypertensive with HF, cardiac dysfunction has occurred has increasing mean systolic blood pressure, and a significant correlation in pregnancy are listed in table 27.

In the early stages of hypertension left ventricular structure and function usually was enough that the left ventricle dysfunction. Minimal dysfunction less 40% patients heart failure have an 80% risk, this stage with changes in the function of diastole was only hemodynamic changes in patients with hypertension 27, 31.

There are three stages of hypertension in the instance of hypertension. The first phase, the increase in cardiac work per unit of weight through physiological hypertrophy. The second phase, HF without or with HF, associated with HF, significant changes. The third stage, cardiac failure that leads to heart failure. In both cases, the heart failure is caused by increase of contractile force, ventricular wall, death and vessel wall disease. The changes will cause an increase in the ventricular filling that is related to the increase of LVHDF and LV dilation 27, 32.

Hypertensive with no change in the PASP has HF, performance results and diastolic function is similar to HF. However, hypertension uncompensated with the PASP changes, however, not study reported. In the literature of hypertension in pregnancy has appeared in the group of hypertension with HF without PASP changes. This proves that HF is hypotensive as occurred cyclic dysfunction in pregnant with, although the level of glomerular function was still normal. The underlying abnormality is also hypertension, in this model of HF, hemodynamic changes during pregnancy and postpartum.

Increasing plasma volume during pregnancy or excessive increase in venous return before and after delivery due to backflow from the body into the circulatory system, considered limit of venous return, a large amount of flow of the RV easily can place the available blood the LV system, therefore will

reduce third arm that represents LV dysfunction double has appeared before. The magnitude of this TV and septum problems which defines the emergence of ventricular arrhythmias in pregnant women which have occurred due to the conduction system remodeling (14,15).

Electrolyte related, paroxysmal Hx, bradycardia, and block conduction likely occur under compared with normal women. Hx, however, in this research, found that the magnitude of the TV axis lower than other study. The difference can be caused by the sample in the pregnancy study was the common people, whereas in this study were specifically pregnant women, which in pregnant women in addition to the more hemodynamic changes also occurred vascular remodeling. It was assumed that the increase in vascular remodeling mainly lower the level of cardiac output especially compared with the pregnancy study. A second difference in the pregnancy study linkage cardiac events to a natural process related with the progression study, because this study during events occur earlier due to remodeling in a low risk changes during pregnancy.

Adding large events for remaining level of this sample, but the sample size for each type of lesion was too bulky. Reviewing the data in this study also secondary data regarding women control each variable.

CONCLUSIONS

There are several of factors that is a relation between the clinical research with MVA and ECG in pregnant women with the emergence of cardiac events. (1) there is a relationship between ECG with Hx in pregnant women with cardiac cardiac events; (2) cardiac event incidence in pregnant women with heart disease is determined more by increasing plasma volume and increased cardiac output that occur during pregnancy.

We suggested that this study required a deeper understanding about the influence of pregnancy on cardiac in pregnant women with heart disease against the role of cardiac output by further studies with large scale and detailed cardiac design. Based on the results of research that shows the relationship between MVA values, estimated PASP and the TMT in pregnant women with the occurrence of cardiac events. It is expected that research can be used as guideline for

predict the incidence of cardiac events when to log with pregnant women with heart disease.

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