ORIGINAL ARTICLE

Assessment of association between pregnancy induced hypertension and cognitive function: Before and after one month of delivery: Cohort study"

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Abstract:

Introduction:

Pre-eclampsia is a leading cause of morbidity and death in mother and baby. This also leads to endothelial dysfunction in large and small vessels, which leads to cognitive impairment. This is the first kind of study from India on the assessment of cognitive function in the Pregnancy-induced hypertension (PIH) group.

Materials and Method:

We recruited cases from the obstetric department's antenatal care. We applied Socio-demographic data and a Cognitive assessment battery (Trail Making Test (TMT) A and B, PGI memory scale, Porteus maze, and Digit Symbol Substitution Test (DSST)) to collect information on cognitive function. The data was collected from May 2021 to November 2021. Assessment was done during pregnancy and one month after Delivery. Data was assessed using SPSS software.

Results:

The TMT A and B values were 27.32 & 57.08 predelivery and 23.34 & 48.74 post-delivery. In PGI memory scale (pre and post-delivery values), Remote memory (6.76 & 6.81), recent memory (4.99 & 5.00), mental balance (6.26 &6.75), attention and concentration(7.42 & 8.27), delayed recall (6.29 &6.9), immediate recall(5.13 & 5.70), verbal retention-dissimilar word (9.52 & 10.18) and recognition (6.75 & 7.62) & DSST (88.0 & 91.31), verbal retention for similar words (5.19 &5.34 &)and visual (2.19 & 2.22) retention. The Maze Test-1 (17.29 & 13.06) Maze Test-2 (21.44 &

16.83). Before Delivery, cognitive impairment was present in the Pregnancy Hypertension (PIH) group in trail making, MAZE test, and certain areas of the PGI memory scale, which were statistically significant (<0.001) compared to the healthy control group. It continues even after one month of Delivery.

Conclusion:

This study has shown that there was an association between the pregnancy-induced hypertensive group and the healthy control group in certain domains of cognitive function before Delivery. The cognitive impairment persists even after one month of Delivery, which signifies microvascular damage persists for a longer duration.

Keywords: *cognitive function, pregnancy-induced hypertension, pre-eclampsia, antepartum, postpartum*

Introduction

According to WHO, Hypertension in pregnancy can significantly affect pregnant women and their babies, which accounts for 14% of maternal-related deaths worldwide. According to WHO, pre-eclampsia is diagnosed when the patient has a new onset of hypertension during pregnancy with diastolic blood pressure ≥ 90 mm Hg and proteinuria (> 0.3 g/24 hours). Eclampsia is diagnosed by the presence of generalized seizures, along with pre-eclampsia criteria. This is because the abnormal vascular response to the placenta leads to widespread endothelial dysfunction in the brain and other organs. In the brain, it can cause stroke, cerebral edema, and intracranial hemorrhage as major events. Sometimes, subclinical microvascular complications lead to changes in attention and concentration and memory problems during pregnancy and after delivery. Removal of the placenta remains the main line of treatment for this condition.[1]

Many pregnant women report changes in focusing attention, remembering things, confusion, and reading difficulties. Collectively, these symptoms are called the "baby brain" phenomenon or, "momnesia." Some studies say that this phenomenon is a myth and that it is due to generalized tiredness rather than actual changes in brain function.

The studies done to assess cognitive impairment by using validated neurocognitive tools have shown conflicting results, with some studies showing worsening cognitive performance, whereas others have shown no difference in cognitive performance when compared with women with normotensive pregnancies.[2,3,4] Radio imaging studies on the brain in PIH women have shown conflicting results again, with some studies reporting increased white matter lesions compared to normotensive pregnancy and some studies reporting no such difference.[4]

The above studies have shown a gap in understanding the association between pregnancy-induced hypertension and cognitive function. Some questions are being raised by the above literature 1) Is there any association between PIH and cognitive function? 2) How long does it persist after the delivery of the baby? In search of answers, we carried out this study. This is the first kind of study from India. The main aim of the study was to find whether there is any association between pregnancy-induced hypertension and cognitive function in the PIH group compared to a healthy control group. We used standard cognitive assessment tools to assess cognitive function.

The following were the aims of the study.

1. To assess the cognitive function during pregnancy in pregnancy-induced hypertension (PIH) group compared to normotensive group."
2. To assess the cognitive function after one-month Delivery of baby, in pregnancy in pregnancy-induced hypertension (PIH) group compared to normotensive group."

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How to Cite this Article:

Santhosh R, Subhashchandra R M, Jayasree J, Mekala B.S. Assessment of association between pregnancy induced hypertension and cognitive function: Before and after one month of delivery: cohort study. Indian Journal of Mental Health and Neurosciences. 2024;7(2):pg 23-30.

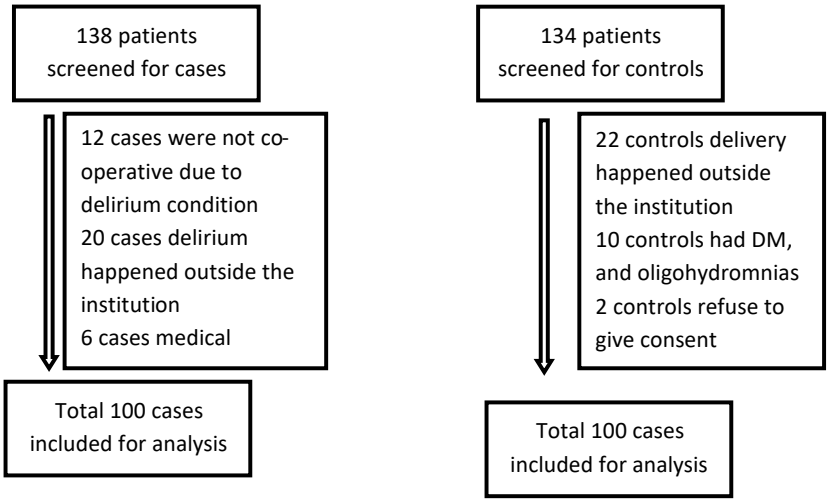
Materials and Methods

After obtaining institutional ethical committee clearance study was started. Informed consent was obtained from patients, and their anonymity was preserved. The data was collected between May 2021 to November 2021.

The method of sample selection was by a sample of convenience. The sample size was calculated using a formula with a power of 0.8 and a ratio of case-healthy control 1.12 probability of an event in case 0.4 and healthy control 0.6.

$$n\ (each\ group) = \frac{(p_0q_0 + p_1q_1)\left(z_{1-\alpha/2} + z_{1-\beta}\right)^2}{(p_1 - p_0)^2}$$

The sample size in the case was 78 and the healthy control was 88, with a total of 166.[1] So, we took a total of 100 patients in the case group (group A) and 100 patients in the healthy control group (Group B).



We recruited all cases (Group A) of pregnancy-induced hypertension (PIH) from the high-risk pregnancy units and age-matched healthy control group (Group B) from regular antenatal OPD dept. of Obstetrics and Gynaecology. We defined pregnancy-induced hypertension (PIH) as if they have pre-eclampsia or eclampsia. Preeclampsia means a pregnant woman has at least one of the criteria. (1) Systolic blood pressure (SBP) >140 mm Hg or diastolic blood pressure (DBP) >90 mm Hg at least 4 hours apart at 20 weeks or more of gestation. (2) new-onset proteinuria, as defined by a urine dipstick 1þ, proteinuria 0.300 g/24 h, or protein/creatinine ratio equivalent to 0.300 g/ 24 h. Eclampsia means epilepsy with pre-eclampsia.

Cognitive assessment was done twice by using the cognitive battery. The first assessment was done in Group A and Group B during pregnancy (7-9 months of pregnancy). The second assessment was done after one month of Delivery of the baby.

The following Tools were used to assess cognitive functions.

Trail Making Test (TMT)-Part-A and B: It's used to assess visual attention and task switching. It gives information about visual search speed, scanning, speed of processing, mental flexibility, working memory, and executive functioning. It has two parts: TMT-A (Root memory) and TMT-B (Executive functioning). Normal values have been established based on age and education. PGI MEMORY SCALE: It's used to assess short-term, and long-term memories. It contains ten subtests - 1)Remote memory, 2)Recent memory 3) Mental balance 4) Attention 5) Delayed recall 6)Immediate recall 7) Retention for similar pairs 8) Retention for dissimilar pairs 9)Visual retention 10) Recognition. Digit Symbol Substitution Test (DSST). It measures a range of cognitive operations. It assesses motor speed, attention, and visuo-perceptual function. It assesses cognitive dysfunction and changes in cognitive function. Adult Porteus Mazes: The Porteus Maze test measures executive functioning, specifically planning and foresight (performance intelligence), for ages three years and over. Inclusion criteria were Pregnancy-induced hypertension with or without pre-eclampsia. Exclusion criteria were patients with a pre-existing mental illness or cognitive impairment or patients with Intellectual Deficiencies. Previous history of Stroke or any other preexisting chronic medical condition was also excluded

STATISTICAL METHODS

The data was analyzed using SPSS -24 version software. To compare prenatal and postnatal data, we used paired t-tests. To assess data between the PIH group and the normotensive group, we used an unpaired t-test

	Mean-Before Delivery	SD	Mean-after Delivery	SD	P value**
TMT-A	27.32	8.391	23.34	2.362	<0.001*
TMT-B	57.08	16.971	48.74	5.993	<0.001*
MAZE TET-1	17.29	4.700	13.06	2.247	<0.001*
MAZE TET-2	21.44	6.007	16.83	4.360	<0.001*
PGI Memory Scale	60.44	5.016	64.52	3.386	0.314
• Remote memory	6.76	0.571	6.81	.465	0.222
• Recent memory	4.99	0.100	5.00	.000	0.317
• Mental balance	6.26	1.070	6.75	.809	<0.001*
• Attention and concentration	7.42	1.499	8.27	.983	<0.001*
• Delayed recall	6.29	1.131	6.90	1.133	<0.001*
• Immediate recall	5.13	.950	5.70	.870	<0.001*
• Verbal retention-similar word	5.19	.901	5.34	.443	0.158
• Verbal retention-dissimilar word	9.52	1.467	10.18	1.298	<0.001*
• Visual retention	2.19	1.089	2.22	.000	0.078
• Recognition	6.75	1.321	7.62	1.080	<0.001*
DSST	88.00	4.267	91.31	3.067	<0.001*

Outliers: Nil. * P value <0.05 means significant
** Paired "t" test was used to calculate "p" value

Table 1. Comparative analysis of cognitive function test in PIH group before and after Delivery (Group A)

RESULTS

The mean age of the PIH group (Group A) was 24.47and the healthy control group (Group B) was 24.84. In the PIH group, 41 % were from urban backgrounds, and 59% were from rural backgrounds, while in the healthy control group, 38% were from urban and 62% were from rural.

The data was presented in the following order. Cognitive function in Group A followed by cognitive function in Group B. Later comparison was done between Group A and Group B during pregnancy followed by after delivery of the baby.

Cognitive analysis of the PIH group (Group A) before and after one month of Delivery of the baby is as follows (Table 1). Some cognitive functions improved after Delivery, while others worsened. TMT A & B and MAZE test function improved after Delivery, while PGI memory and DSST continued to worsen after one month of Delivery. The TMT A and B show predelivery values are 27.32&57.08 and after-delivery values are 23.34 & 48.74 (Table 1). The difference was statistically significant. In the PGI memory scale, the following test worsens following Delivery. Remote memory (6.76 & 6.81), recent memory (4.99 & 5.00), mental balance (6.26 &6.75), attention and concentration (7.42 & 8.27), delayed recall (6.29 &6.9), immediate recall (5.13 & 5.70), verbal retention-dissimilar word (9.52 & 10.18) and recognition (6.75 & 7.62) & DSST (88.0 & 91.31), verbal retention for similar words (5.19 &5.34 &)and visual (2.19 & 2.22) retention (Table 1). The MAZE TET-1 (17.29 & 13.06) and MAZE TET-2 (21.44 & 16.83), there was a decreasing trend. PGI memory score and digit symbol substitution test continue to worsen even after Delivery, while trail making and maze test continue to improve (Table 1).

In the healthy control group (Group B)(Table 2), the PGI memory test and MAZE test show improved cognitive function tests, while trail-making and DSST show worsening cognitive function following Delivery. Except for the MAZE test, none of them were statistically significant. The TMT A (18.73 &18.85) and B (45.76 & 45.81) show no significant difference between pre and post-delivery (Table 2). In the PGI memory scale, the following test continues to normal following Delivery. Remote memory (6.65 & 6.72), recent memory (4.97 & 4.98), mental balance (6.26 &6.29), attention and concentration (7.20 & 7.59), delayed recall (5.68 &5.64), immediate recall (5.06 & 5.45), verbal retention-dissimilar word (8.18 & 8.29) and recognition (6.2 & 6.14) & DSST (89.22 & 89.24) Table 2). In verbal retention for similar words (4.51 & 4.44) and visual (2.09 & 1.53) retention (Table 2). In MAZE TEST-1 (13.13 & 11.76) and MAZE TEST-2 (14.9 & 13.36), there was a statistical difference between the pre and post-test (Table 2).

	Mean-Pre-delivery	SD		Mean-Post delivery	SD	P** value
TMT-A	18.73	2.681		18.85	2.472	0.964
TMT-B	45.76	3.610		45.81	3.776	0.465
MAZE TET-1	13.13	1.212		11.76	1.232	<0.001*
MAZE TET-2	14.90	1.744		13.36	1.396	<0.001*
PGI Memory Scale	59.19	3.675		59.21	3.548	0.692
• Remote memory	6.65	0.557		6.72	.362	0.317
• Recent memory	4.97	0.300		4.98	.141	0.655
• Mental balance	6.26	0.655		6.29	.640	0.059
• Attention and concentration	7.20	1.243		7.59	1.288	0.790
• Delayed recall	5.68	1.024		5.69	1.040	0.346
• Immediate recall	5.06	0.833		5.45	.859	0.585
• Verbal retention-similar word	4.51	0.785		4.58	.783	0.345
• Verbal retention-dissimilar word	8.18	1.8		8.29	1.641	0.375
• Visual retention	2.09	1.010		2.10	1.049	0.071
• Recognition	6.20	1.025		6.41	.779	0.499
DSST	87.22	2.464		89.24	2.539	0.713

Outliers: Nil, *P value <0.05 means significant
** Paired "t" test was used to calculate "p" value

Table 2. Comparative analysis cognitive function in Healthy control group before and after Delivery (Group B)

During pregnancy:

A comparison between the PIH group (Group A) and the healthy control group (Group B) (Table 3) during pregnancy showed an overall worsening of cognitive function in group A. In all the parameters of cognitive domains, the mean score was higher in the PIH group (Group A) compared to the healthy control group (Group B). In the trial-making and MAZE tests, the cognitive dysfunction was statistically very significant (<0.001). The following are the cognitive parameters that were statistically significant. Those are TMT-A (27.32 & 18.73), TMT-B (57.08 & 45.76) delayed recall (6.29 & 5.68), immediate recall (5.13 & 5.75), verbal retention-similar word (5.34 & 4.51), verbal retention-dissimilar word (9.52 & 8.18) & MAZE TET-1 (17.29 & 13.13) MAZE TET-2 (21.44 & 14.90) (Table 3). The following test did not get much affected by PIH. Remote memory (6.76 & 6.85), recent memory (4.99& 4.97), mental balance (6.26 & 6.34), attention and concentration (7.42 & 7.64) & DSST (88.00 & 89.22) (Table 3).

	During pregnancy			One month after Delivery		
	Pregnancy Induced Hypertension Group (Group A)	Healthy control group (Group B)	P Value	Pregnancy Induced Hypertension group	Healthy control group	P value **
TMT-A	27.32	18.73	<0.001	23.34	18.65	<0.001*
TMT-B	57.08	45.76	<0.001	48.74	45.51	<0.001*
MAZE TET-1	17.29	13.13	<0.001	13.06	11.76	0.258
MAZE TET-2	21.44	14.90	<0.001	16.83	13.36	<0.001*
PGI Memory Scale	60.44	59.19	0.046	64.52	59.21	<0.001*

	During pregnancy			One month after Delivery		
	Pregnancy Induced Hypertension Group (Group A)	Healthy control group (Group B)	P Value	Pregnancy Induced Hypertension group	Healthy control group	P value **
• Remote memory	6.76	6.65	0.261	6.81	6.72	<0.001*
• Recent memory	4.99	4.97	0.528	5.00	4.98	<0.001*
• Mental balance	6.26	6.26	0.524	6.75	6.29	<0.001*
• Attention and concentration	7.42	7.20	0.260	8.27	7.59	<0.001*
• Delayed recall	6.29	5.68	<0.001	6.90	5.69	<0.001*
• Immediate recall	5.13	5.06	<0.001	5.70	5.45	<0.001*
• Verbal retention-similar word	5.19	4.51	<0.001	5.34	4.58	<0.001*
• Verbal retention-dissimilar word	9.52	8.18	<0.001	10.18	8.29	<0.001*
• Visual retention	2.19	2.09	<0.001	2.22	2.10	<0.001*
• Recognition	6.75	6.20	<0.001	7.62	6.41	<0.001*
DSST	88.00	87.22	0.015	91.31	89.24	<0.001*

**Independent "t" test was used calculate the "p" value
Outliers: Nil, *P value <0.05 means significant

Table 3. Comparative analysis of cognitive function between PIH and Healthy control group before and after Delivery (group A and group B) (N=100)

AFTER ONE MONTH OF DELIVERY OF THE BABY

Comparison between the PIH group (Group A) and the healthy control group (Group B) showed statistical differences in all the areas except MAZE TET 1(Table 3). Though certain areas in cognitive domains improved following Delivery in the PIH group compared to the healthy control group, the PIH group had more cognitive dysfunction (Table 3).

DISCUSSION

This study has shown that cognitive impairment can happen during PIH (Group A) in pregnant patients compared to the healthy control group (Group B). Cognitive impairment continues to occur after one month of Delivery of a baby among these groups (Table 1&2). This study has shown that cognitive impairment will not affect all the domains of mental function.

The following were the significant findings from this study. First, there is a trend toward cognitive impairment in PIH (Group A) than the healthy control group (Group B). Second, women with PIH showed impairment in multiple domains of cognitive impairment, most prominently affecting frontal lobes like brain processing, executive functioning, verbal learning, and attention (Table 1).

The Trail making test and MAZE test were maximally affected during pregnancy (Group A) compared to the healthy control group. Trail-making showed impairment in visual attention, search speed, task switching, scanning, speed of processing, mental flexibility, and executive function (Table 1).

The study by Julie A found that impairment in Trail Making Test B. The changes observed were in the following domains. Cognitive speed and flexibility, executive function (d ¼ 1.96), verbal learning (d ¼ 1.93), visual memory (d ¼ 1.87), auditory attention (d ¼ 1.69).[4] Our study also showed changes in the Trail-making test suggesting this can be used as one of the important tools to assess cognitive function in PIH patients (Table 1).

The Porteus Maze test measures executive functioning (planning and foresight). This also affected maximally in our study. Following Delivery, there was an improvement in test performance in the PIH group, but it was still high compared to the healthy control group Table 1 & 2). This suggests PIH affects planning, foresight, and executive function.

In the PGI memory test, memory impairment was not that much affected during pregnancy compared to the Delivery in the PIH group (Table 1). However, retention and recognition were affected more. The study by Natalie Dayan et al. 2018 said that memory was not affected that much compared to the healthy control group.[5] In another recent study, cognitive functioning was studied before and after the Delivery of the baby in pre-eclamptic patients and healthy controls (Table 3). In this study, pregnant women had more changes in memory compared to non-pregnant healthy control patients. After the delivery of the baby, there were no much statistical differences in both groups in terms of memory and attention.

In DSST (measures attention), we found a worsening performance in pregnant women in both PIH and healthy control groups and it was statistically significant (Table 3). A similar finding was present even after the delivery of the baby. A meta-analysis by Malik Elharram et al. 2018 found that there was no significant difference between patients with and healthy control groups in DSST score.[1] Worsening of attention is an important finding in our study compared to pooled data analysis from Malik Elharram et al. 2018.

The underlying mechanism involved was micro-vascular and macro-vascular changes in the blood flow can cause structural and functional changes in the brain, leading to cognitive impairment directly or indirectly by altering white matter pathways.[6,7] This impairment was probably due to cerebral ischemia and edema in the clinical phase of the disease.[8] The memory deficits are permanent because radiological imaging has shown permanent damage in the white matter and loss of volume in the hippocampus and thalamus in eclamptic fit patients.[9] Some studies have shown lesions in temporal and frontal white matter, a decrease in cortical gray matter volume, and shrinkage in total brain volume in the PIH group.[10-13]

The other explanation for memory changes is due to hormonal system changes during pregnancy. Ali SA 2018 showed that hormonal changes affect cognitive performance.[14-16] They report that estrogen has a role in neuroprotective effects on degenerative disease or injury. The altering level of estrogen has led to changes in cognitive function.

The strength of this study was the assessment of cognitive function during pregnancy and one month after the delivery of the baby. We used standard tools to assess cognitive dysfunction. Sufficient sample size was used. We took the healthy control group to see if there was any difference in the trend in the healthy control (Group B) and case groups (Group A).

Limitations of this study were no long-term follow-up. We did not include other cardiovascular risk factors like obesity, smoking, elevated cholesterol levels, diabetes status, and severity of antenatal hypertension, which affects micro-vessel and macro vessels.

CONCLUSION

This study has shown that there was an association between the pregnancy-induced hypertensive group and the healthy control group in certain domains of cognitive function before Delivery. The cognitive impairment persists even after one month of Delivery, which signifies microvascular damage persists for a longer duration. It's because PIH leads to short-term and long-term cognitive impairment and effective management of PIH and subsequent preventive measures helps to prevent dementia and other cognitive impairments.

ACKNOWLEDGEMENTS

Nil

SOURCE OF FUNDING

Nil

CONFLICT OF INTEREST

Nil

AUTHOR'S CONTRIBUTIONS

Dr. Santosh Ramdurg has contributed to forming a research idea, data collection, analysis, and script writing. Dr S R Mudanur has contributed to forming a idea, collecting data, and writing scripts. Dr Mekhala Bhargava Swaraj has contributed to data collection. All the authors have approved the final script.

CONSENT

As per the ICMR guidelines, the informed written consent has been obtained and preserved by the corresponding author.

ETHICAL APPROVAL

As per the National standards, the ethical approval letter/ certificate from local IEC has been obtained and preserved by the authors.

FINANCIAL DISCLOSURE

Nil

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