



# GESTATIONAL EXPOSURE TO ANTIDEPRESSANTS AND THEIR IMPACT ON THE NEURODEVELOPMENT AND PHYSICAL OUTCOMES IN THE OFFSPRING: A POPULATION-BASED COHORT STUDY

Pallavi singh, Dr P Geetha \*

Corresponding Author: Dr P Geetha

Assistant professor

Department of pharmacy practice

Vels institute of sciences and technology, Chennai, pallavaram

Author 1: Mrs Pallavi Singh

Research scholar

Department of pharmacy practice

Vels institute of sciences and technology, Chennai, pallavaram

Email id: [pallavisingh090@gmail.com](mailto:pallavisingh090@gmail.com)

## ABSTRACT:

This study is aimed to study the gestational exposure to antidepressants and their impact on the neurodevelopment and physical outcomes in the offspring. The objective of the study is to General and medical information, as well as estimations of the level of mental distress will be obtained by standardized questionnaires. To access the prevalence of antidepressant associated symptoms in new born Assessment of Neurodevelopment and physical outcomes of child by using standardized questionnaires namely Early Motor Questionnaire (EMQ) for age group of children from 1-6 years which is parent questionnaire were circulated to control (n-250) and case (n-250). Physical outcomes like congenital malformations, birth weight, seizures, hospitalization, preterm delivery, respiratory distress of children were collected from retrospective data maintained during gestational period and child birth which were collected from clinic.

**Results and discussion:** In pregnant women baseline risk of congenital malformations is about 3%, and of cardiovascular malformations, 1%. Rates of spontaneous abortion vary in general population between 15 and 20%. Pre-term births occur in approximately 13% of pregnancies, we found relation between



exposure of prenatal antidepressants and occurrence of physical outcomes like low birth weight, miscarriages, hospitalization, preterm births, respiratory distress, seizures, gastrointestinal problems, improper. Neurodevelopment abnormalities were found in the case as a result of serotonergic toxicity and withdrawal symptoms of antidepressants in offspring. During follow up of study the children's Gross motor skills, Fine motor skills, Perception action and mental cognition were analyzed using EMQ questionnaires and their scores were compared with control and significant result was found.

**Conclusion:** Based on observations made in this study, neonatal outcomes were observed; the withdrawal symptoms experienced by the child were transient and also alter lifestyle.

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## INTRODUCTION

Pregnancy and the birth of a child both are considered as very joy full opportunity, but it can be full of challenges for many mothers. Pregnant women usually experience depressive mood in their early pregnancy and also during child birth. The actual phenomenon is the trigger of larger hormonal fluctuation which is occurring during the time of pregnancy. Many studies found out the depression not only affect the pregnant women it also effects the infants physical and cognitive development. Studies also suggested that if the gestational depression is not diagnosed early it can lead very serious condition during the postpartum period. Many short term and long term adverse effect in seen in children who may suffer from antenatal depression which includes the increased risk of low birth weight, preterm birth or even emotional problem and other mental issues in later childhood and adolescence. When the anti depression crosses the placenta and the blood brain barrier and also passes into the breast milk which increases the mediator levels in the fetus who are developing and also it effects the functional development of the brain which effect the neurobehavioral activity, cognitive and mental disorders, which can affect the further development of the child , with this finding our research was aimed to study the antidepressants exposure during gestation and their impact on the neurodevelopment and physical outcomes in the offspring

### Aim & objectives:

A retro- prospective analysis to study the gestational exposure to antidepressants and

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their impact on the neurodevelopment and physical outcomes in the offspring: a population-based cohort study. General and medical information, as well as estimations of the level of mental distress will be obtained by standardized questionnaires. To access the prevalence of antidepressant associated symptoms in new born

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**Plan of work:** Study design, Literature review, Submission to ethical committee, Retrospective Data collection, Subject enrollment, Statistical analysis, Intervention, Thesis writing, Submission of report

### Materials and Methods:

A population-based retro-prospective study conducted in Chennai with the retrospectively collected data from the psychiatrists is observed in a comparative manner including two groups 500 mothers among which 250 were of controls (mothers not exposed to antidepressants during their pregnancy) and 250 are the cases (mothers exposed to antidepressants during their pregnancy) from whom the follow up has been taken. Both the groups are compared to each other to investigate the relationship between the medication exposure and incidence of physical outcomes and cognitive impairment of offspring. The retrospective data was collected from the year 2010-2020 from a private hospital in Chennai Tamilnadu

The primary objective of the study is to assess the neurodevelopment of the child using standardized questionnaires Early Motor Questionnaire [18] (EMQ) for the age group of

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children from 1-6 years which is a parent questionnaire. The physical outcomes like congenital malformations, birth weight, seizures, hospitalization, preterm delivery, respiratory distress of the children were noted from the previous records maintained during the child birth which were collected from the clinic. The EMQ questionnaire used 5-point scale which is ranging from -2 to +2 for the parents. The behavior is rated 2 if the parent is sure that the child does not show the behavior yet and 2 if parent remembers a particular instance where the child exhibited the behavior in question. Further, the EMQ is divided into 3 sections, a Gross Motor section (49 items), a Fine Motor section (48 items), and a Perception-Action section (31 items). Approval was obtained from an Institutional Ethical Committee, Vels Institute of Science Technology and Advanced studies, Chennai to carry out this study. Ethical Committee reference number is VISTAS-SPS/IEC/VI/2020/13. Based on the

inclusion and exclusion criteria the subjects were included in the study. The EMQ questionnaire for both case and control was compared by chi square test using spss.

**Exposures**

From 2010-2020 among the case population,

52 women exposed to Sertaline, 25 exposed to Venlafexine, 19 exposed to Paroxetine, 18 exposed to Fluoxetine, 18 exposed to the combination of Venlafexine and Mirtazepie and 18 exposed to Escitalopram. The length of Antidepressant medication in pregnant women goes like, 83 mothers took it throughout pregnancy, 82 between the 1<sup>st</sup> and 6<sup>th</sup> trimesters and 22 only on the first three trimesters as compared to the non-exposed group mothers who aren't exposed to any antidepressant drugs were taken into the study.

**Fig1. Antidepressants prescribed in the study population.** The distribution of the use of different classes of antidepressant drugs in the exposed mothers.

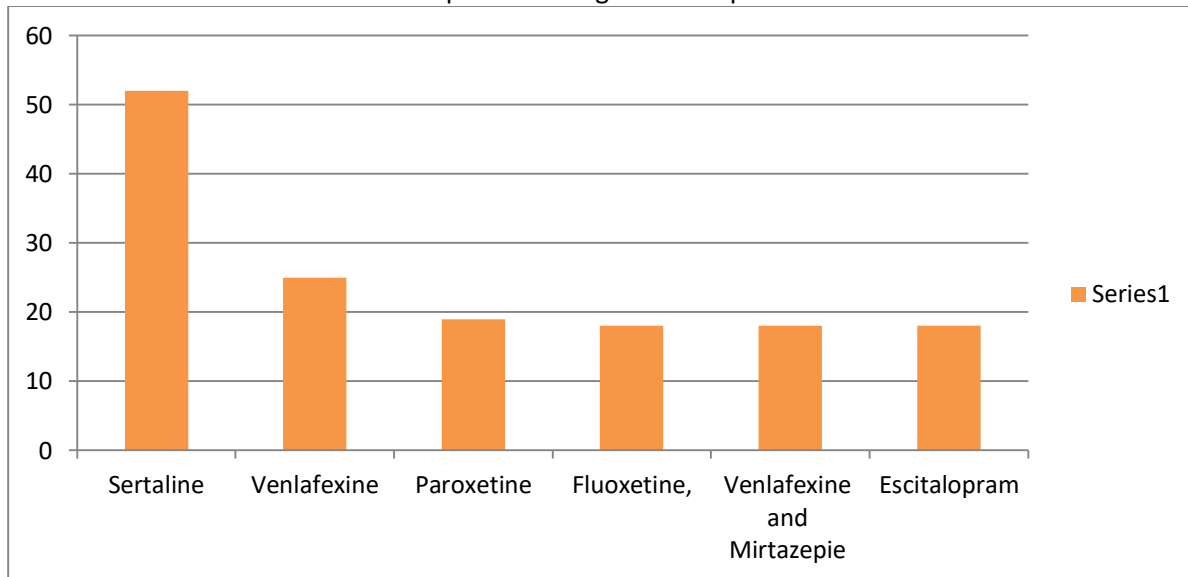


Table 1 shows the incidence of each outcome in both the groups, the relative risk and their significance level (P values). As the p-values of all the parameters observed are greater than 0.005 (95% CI) there is no significant difference found in both the groups.

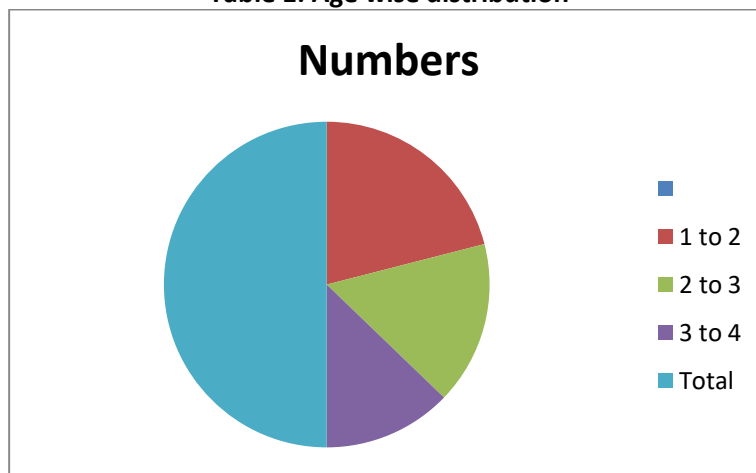


**RESULTS AND DISCUSSION**

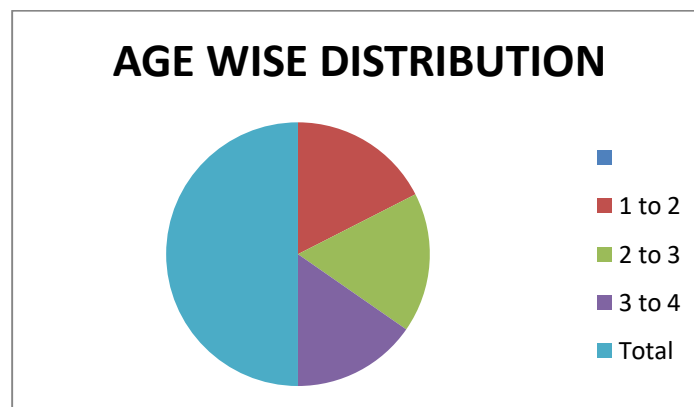
Out of the selected 300 participant, 105 (35%) children were under the age of 1-2 years, 103 (41.5%) were under the age of 2-3 years and 92 (42.3%) was under the age of 3-4 years. (Table 1, figure 1)

Category	Numbers	percentage
1 to 2	210	35
2 to 3	162	65.32258065
3 to 4	128	84.67741935
Total	500	

**Table 1: Age wise distribution**



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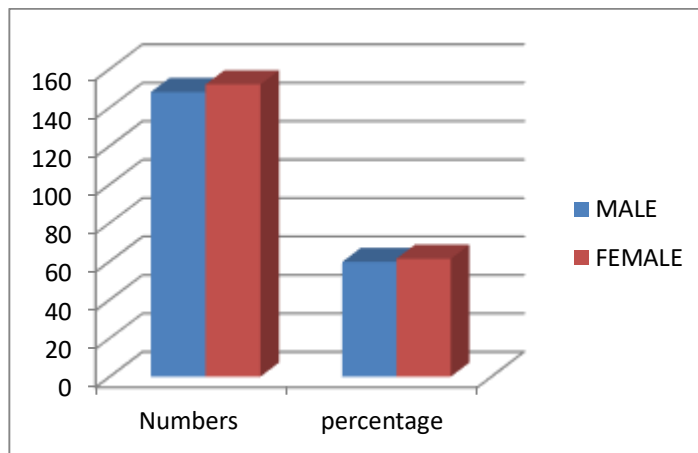
**Fig1: Age wise distribution**

Out of the selected 300 participants 148 (59.6%) children was male and 152 (61.2%) was female (Table 2, figure 2)

**GENDER**

Category	Numbers	percentage
MALE	248	100
FEMALE	252	101.6129032
TOTAL	500	

**Table 2: Gender wise distribution**



**Fig2: Gender wise distribution**

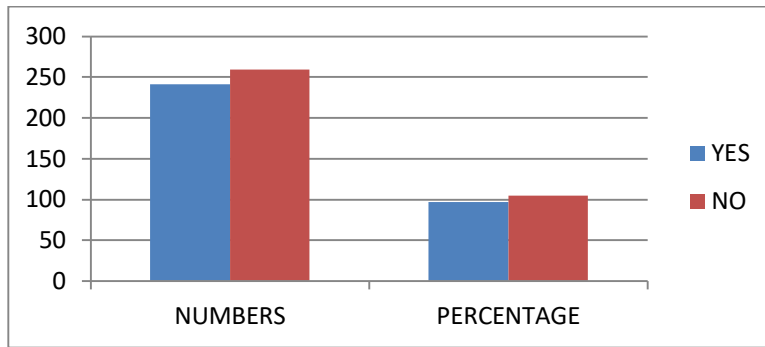
Out of the selected 500 patients 241 (97.177%) were premature infants and 259 (104.4%) were not premature infants (Table 3, figure 3)

**PREMATURE DELIVERY**

CATEGORY	NUMBERS	PERCENTAGE
YES	241	97.17741935
NO	259	104.4354839
TOTAL	300	



**Table 3: Premature infant**



**Figure3: Premature infant**

While comparing the EMQ questionnaires of the case with control for all the three sections (gross motor skill, fine motor skill and perception motor skill) we found significant results by using Pearson chi square test.

**GROSS MOTOR SKILL**

**Chi-Square Tests**

	Value	df	Asymp. Sig. (2-sided)
Pearson Chi-Square	541.439 <sup>a</sup>	6	.000
Likelihood Ratio	69.089	6	.000
N of Valid Cases	501		

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*a. 9 cells (50.0%) have expected count less than 5. The minimum expected count is .00.*

**Chi-Square Tests**

	Value	df	Asymp. Sig. (2-sided)
Pearson Chi-Square	509.043 <sup>a</sup>	6	.000
Likelihood Ratio	22.533	6	.001



<b>FINE MOTOR SKILL</b>	N of Valid Cases	501		
	<i>a. 9 cells (50.0%) have expected count less than 5. The minimum expected count is .00.</i>			

**PERCEPTION MOTOR SKILL**

**Chi-Square Tests**

	Value	df	Asymp. Sig. (2-sided)
Pearson Chi-Square	505.242 <sup>a</sup>	8	.000
Likelihood Ratio	19.825	8	.011
N of Valid Cases	501		

*a. 9 cells (50.0%) have expected count less than 5. The minimum expected count is .00.*

**Discussion**

Previous animal studies showing the risk of neonatal outcomes, congenital malformations and early growth and development issues were taken into consideration even though they are not completely reliable. The decision expose the fetus to antidepressant medication during pregnancy must be weighed against the risks of untreated maternal depression to both mother and fetus. In our study the mothers coming under the case exposed to antidepressants were the ones diagnosed with major depressive disorder and prescribed with antidepressants will be sufficient for mild to moderate depression.

Among the women who were exposed to antidepressants most of the mothers were medicated throughout the pregnancy and were still continuing the medication at the time of the study because depression in many cases is long lasting and has to be treated for a longer period in the lifespan of patients. We initiated this study with the aim to analyze any

neurodevelopment changes and other physical outcomes occurring in children exposed to prenatal antidepressants and the comparison of the same with the unexposed population. The incidence of unpleasant outcomes as it was observed in the general population and exposed group are reported in our study. The observed etiologic factors of such outcomes in the current study are probably due to history of psychiatric disorders, older age of mothers or fathers, and psychiatric disorders in the mother before pregnancy.

The general population baseline risk of congenital malformations based on the literature review is about 60-70%, and of cardiovascular malformations 35%. 68% rates of spontaneous abortion vary in the general population. Pre-term births occur in approximately 52% of pregnancies. Neonatal outcomes, such as poor neonatal adaptation and persistent pulmonary hypertension of the newborn (PPHN) also have a baseline incidence



in the general population, as do impaired developmental outcomes.[19]

With the proper statistical analysis, we found the relation between the exposure of prenatal antidepressants and the occurrence of physical outcomes like low birth weight, miscarriages, hospitalization, preterm births, respiratory distress, seizures, gastrointestinal problems, improper

Neurodevelopment was assumed to occur as a result of serotogenic toxicity and withdrawal symptoms of antidepressants in the offspring. During the follow up of the study the children's Gross motor skills, Fine motor skills, Perception action were analyzed using EMQ questionnaires and their scores were compared with unexposed group.

The analysis says there is significant difference found between both the groups in case of neurodevelopment and other observed physical outcomes. From the other observations made in the current study we state that there may be a significant difference in the occurrence of depression in the early adolescence of children with depressed mothers, secondly the postpartum depression episodes in the mothers were severe. We recommend the use of SSRIs, SNRIs and other class of Antidepressants like mirtazapine in pregnant mothers was having mild risk. In summary we state that prenatal exposure of antidepressants is not acceptable and cause significant harm to the developing child compiling with previous studies stating the same. The neonatal outcomes reported retrospectively and the follow up taken from those children of exposed mothers concludes that they are withdrawal symptoms which are transient and alter the lifestyle of the children permanently.

#### Conclusion:

Even in the current medical scenario there is still an uncertainty on use of antidepressants in pregnant women. Based on observations made in this study and by calculating the motor skills (gross motor, perception motor skill and fine

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motor skill) we found significant difference and the neonatal outcomes were observed with the withdrawal symptoms experienced by the child were transient and also alter lifestyle.

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