

## Original Research Article

# Is hormonal contraceptive risk for congenital malformation?

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### ABSTRACT

**Background:** Little research is conducted in the safety of emergency contraceptives so the potential for developmental toxicity has not been evaluated.

**Methods:** This hospital based descriptive study was conducted at tertiary care center, Krishna Hospital. Mothers who are diagnosed to have congenital birth defected fetus through antenatal examinations, delivered baby with diagnoses of congenital malformation, congenital malformed admitted neonates at Tertiary care hospital or came for reference services were assessed from September 2016 to August 2017.

**Results:** The prevalence with number of birth, it is 1.4% and calculating with number of neonates admitted its prevalence rate is 5.3%. Overall in the hospital the prevalence noted is 0.2%. 283 mothers were diagnosed to have congenital malformation baby, among these, 264 (93.3%) mothers not had any history of birth control pills use and only 19 (6.7%) mothers stated that they used the birth control pills. Those used birth control pills in those 4 babies (1.4%) born with nervous system defects, 3 babies (1.1%) had cleft lip and cleft palate, and 2 (0.7%) babies had digestive system, musculoskeletal system and chromosomal abnormalities. Association between congenital malformation and history of Use of birth control pills shows strong association.

**Conclusions:** The problem of conclusively proving a small increase in the incidence of rare abnormalities is very formidable. This may be due in part to the fact that the anomalies associated with hormonal contraceptives may occur primarily in those children who are predisposed genetically.

**Keywords:** Hormonal contraceptive, Risk factor, Congenital malformation

### INTRODUCTION

A woman's ability to choose if and when to become pregnant has a direct impact on her health and well-being. Contraceptive pills have been a revolutionizing factor in the field of family planning. The pill, which contains either estrogens alone or an estrogen progestogen combination, is the most effective method of contraception, and its wide use can reduce the growth of population considerably. Hormonal contraceptive are most commonly used spacing methods. Oral

contraceptive pills or birth control pills are hormonal preparations comprising of synthetically prepared estrogen and progesterone hormones or only progesterone. They impede the functioning of natural hormones and inhibit the secretion of follicle stimulating hormone (FSH) and luteinizing hormone (LH) which are required for maturation of eggs and preparation of uterine lining for embryo implantation. Contraceptive pills interfere with implantation and fertilization of eggs and thus prevent pregnancy. Due to their high efficacy, they are increasingly used by women all over the world to

prevent unwanted pregnancies. Knowledge and research on safety concerning with use of contraceptive pill is very limited. Decades of research on contraceptives shows association of developing vaginal malignance tumor. Very limited studies are available on the relation between oral contraceptive pills use just before or during pregnancy and its effect on fetal development. It's still not clear that how long potential effects of these drugs lasts. Although the majority of previous studies have reported no association between OC use during pregnancy and birth defects, some studies have reported increased occurrence of neural tube defects, limb reduction defects, and urinary tract anomalies.<sup>1</sup> There has been some evidence that teratogenic potential still remains even after the contraceptive are discontinued prior to pregnancy.

There are two possible hypotheses proposed by Dr. Lalit ambani, which explain mechanism of contraceptive hormones producing malformations.<sup>14</sup> One hypotheses state that the contraceptive hormones have direct effect on gene mutation causing development of a specific malformation. Other hypothesis explains that Low metabolic clearance of the hormones lead to abnormal accumulation and acts as toxic to the embryo either directly or by reducing the availability of vitamins crucial to fetal growth, such as folic acid. Philip explained hormonal contraceptives; both progestogens and estrogens have been implicated as teratogens as well as mutagens in individual germ cells and when child subsequently conceived with that germ cell would be anomalous.<sup>3</sup>

Emergency contraceptive is another aspect needed to be evaluated its effect on birth defects. The most common available emergency contraceptive regimens are high-dose estrogen, danazol, mifepristone, an estradiol-levonorgestrel combination, and levonorgestrel. World health organization has conducted large-scale clinical trial and stated that levonorgestrel as the gold standard in hormonal emergency contraception because of its improved tolerance and efficacy.<sup>2</sup> Little research is

conducted in the safety of emergency contraceptives so the potential for developmental toxicity has not been evaluated.

## METHODS

This hospital based descriptive study was conducted at tertiary care center, Krishna Hospital, attached to Krishna Institute of Medical Sciences "Deemed to Be University", Karad Maharashtra state, India. The aim of the study was to evaluate the prevalence and risk factors of congenital malformation. Mothers who are diagnosed to have congenital birth defected fetus through antenatal examinations, delivered baby with diagnoses of congenital malformation, congenital malformed admitted neonates at Tertiary care hospital or came for reference services were assessed from September 2016 to August 2017. Total 75136 babies were observed in pediatric outpatient department, 4092 babies in pediatric ward and 774 patients in neonatal intensive care unit.

## RESULTS

In the present study researcher have gathered the data from two units, Pediatric unit and Maternity unit. Pediatric unit included pediatric outpatient department, pediatric ward and Neonatal Intensive Care Unit where 80002 patients were assessed. Prevalence is noted maximum in the neonatal intensive care unit 41 (5.3%), thereafter in pediatric ward 14 (0.3%), and in pediatric outpatient department 45 (1%). Maternity unit included maternity outpatient department, maternity ward which also included labor room. In the maternity outpatient department 50856 patients were visited in that 131 patients had the diagnosis of having congenital malformation fetus contributing to 0.3%. Whereas maternity ward had 3847 patients among those 52 (1.4%) had delivered congenital malformed babies. In our study considering the prevalence with number of birth, it is 1.4% and calculating with number of neonates admitted its prevalence rate is 5.3%. Overall in the hospital the prevalence noted is 0.2%.

**Table 1: Prevalence of congenital malformation.**

Area including inpatients and outpatient department	Total patients attended	Numbers of congenital malformation	Percentage (%)
<b>Total in pediatric units</b>	80002	100	0.12
<b>Total in maternity unit</b>	54703	183	0.33
<b>Overall prevalence in hospital (Total)</b>	134705	283	0.2

The Table 2 explains congenital malformation and history of Use of birth control pills. 283 mothers were diagnosed to have congenital malformation baby, among these, 264 (93.3%) mothers not had any history of birth control pills use and only 19 (6.7%) mothers stated that they used the birth control pills. Those used birth control

pills in those 4 babies (1.4%) born with nervous system defects, 3 babies (1.1%) had cleft lip and cleft palate, and 2 (0.7%) babies had digestive system, musculoskeletal system and chromosomal abnormalities. Association between congenital malformation and history of Use of birth control pills shows strong association.

**Table 2: Association of congenital malformation with use of birth control pills.**

System of congenital malformation	Use of birth control pills		
	No	Yes	Total
<b>Congenital malformations of the nervous system</b>	59	4	63
<b>Congenital malformations of eye, ear, face and neck</b>	2	0	2
<b>Congenital malformations of the circulatory system</b>	51	6	57
<b>Congenital malformations of the respiratory system</b>	5	0	5
<b>Cleft lip and cleft palate</b>	26	3	29
<b>congenital malformations of the digestive system</b>	21	2	23
<b>Congenital malformations of genital organs</b>	19	0	19
<b>Congenital malformations of the urinary system</b>	21	0	21
<b>Congenital malformations and deformations of the musculoskeletal system</b>	45	2	47
<b>Other congenital malformations</b>	2	0	2
<b>Chromosomal abnormalities, not elsewhere classified</b>	13	2	15
<b>Total</b>	264 (93.3%)	19 (6.7%)	283

## DISCUSSION

Malformation depends on many such as the specific agent (teratogens) used and its dosage, the time point in gestation during which the fetus was exposed, and the genetic susceptibility of the mother and the fetus. More relevant clinically are allegations that oral contraceptives are associated with cardiac defects, limb reduction defects, neural tube defects, hypospadias, and other anomalies.<sup>3</sup> Levy and associates were the first to claim that progestins cause cardiac anomalies.<sup>4</sup> Similar results were shown by Nora and Nora, Gal et al reported the relation between use of birth control pill and neural tube defect, even after excluding the other risk factors such as mother chronic diseases, advanced age and other predisposing factors.<sup>4,5</sup> Levy et al noted a high incidence of hormone treatment in pregnancies leading to the birth of infants with transposition of great vessels.<sup>6</sup> Similar observations are made by Nora and Nora, Mulv hill et al.<sup>7,8</sup> Brogan reported the risk for developing cleft lip and palate.<sup>9</sup> Janerich et al reported limb defect would be the risk for receiving hormonal therapy.<sup>10</sup> Spira et al found that malformation rate are almost equally frequent in hormonal exposed and unexposed pregnancies.<sup>11</sup>

There are many studies shows no co relation between congenital malformations and former contraceptive pill-users.<sup>12,13,15-21,23</sup>

In our result, we found maximum (93.3%) malformation were in those woman who has never exposed to hormonal contraceptives, and only 6.7% were diagnosed to have malformation with history of contraceptives use. As yet, there is no clear and definitive evidence on effects of oral contraceptives administered prior to or during pregnancy on malformations. Reviewing literature also shows contradictory results as exposure time duration before and during pregnancy is not mentioned accurately due to memory bias of mothers included in study, which is weakness of our study too. For women who have a breakthrough pregnancy during oral contraceptive use or

even intentionally become pregnant within a few months of stopping oral contraceptive use, any exposure is unlikely to cause her fetus to develop a major birth defect. There is no literature demonstrating any heterogeneity in the risk of birth defects by oral contraceptive formulations. Many women may take contraceptive. According to some studies folate lacking is strongly linked to neural defect but in our study we asked mother who had malformation and taken contraceptives about folic acid intake. All mother were had antenatal registration and prescribed folic acid right from the pregnancy. Hence folate deficiency is not directly linked to malformation but it may be due to hypotheses that contraceptives may decrease folate availability.

The problem of conclusively proving a small increase in the incidence of rare abnormalities is very formidable. This may be due in part to the fact that the anomalies associated with hormonal contraceptives may occur primarily in those children who are predisposed genetically.

### Limitations

Appropriate prospective surveys to study the pregnancy of women who had used hormonal contraceptives during or before pregnancy could give us much more definitive data. In understanding the exact effect of oral contraceptive as a teratogens effect on malformations it would be better to consider duration of exposure and exposure to progestogens only, estrogens only, and combined oral contraceptives. Duration of exposure of contraceptives before pregnancy is much important as low metabolic clearance of the hormones lead to abnormal accumulation of hormones effecting fetal development.

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