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Research Article

# Does *In Vitro* Fertilization Newborns Showed More Risk for Malformations?

**Jorge Sales Marques[1,2]***

[1]*Centro Hospitalar Conde S. Januário, Macau, China*
[2]*Hospital Cuf Trindade, Porto, Portugal*

***Corresponding Author:** Jorge Sales Marques, Centro Hospitalar Conde S. Januário, Macau, China and Hospital Cuf Trindade, Porto, Portugal.

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## Abstract

*In vitro* fertilization (IVF) refers to a procedure designed to overcome infertility and produce a pregnancy as a direct result of the intervention.

We reviewed all newborns admitted in NICU during a period of five years. There was a total 2875 cases.

Of these, 68 were IVF newborns.

The purpose of the study was to see how many newborns showed malformations, compared with other non-IVF group and related this finding with the gestational age, birth weight and common complications of prematurely like hyaline membrane disorder (HMD) and necrotizing enterocolitis (NEC).

The gestational age (GA) of IVF newborns admitted in NICU was mainly between 32-36W+6 and their birth weight (BW) was between 1.5 and 2.5 kg.

Four of the IVF newborns admitted to NICU had congenital malformations (The rate was 5.8%) compared with zero cases in non IVF group. This result was statistically significant. The malformations detected were: duodenal atresia, anal atresia, cleft lip and palate, ventricular septal defect.

The incidence of prematurity, low birth body weight, short term complications (HMD, NEC) and long hospital stays in IVF group is higher than non-IVF group and are also statistically significant.

The mortality rate of both groups was statistically not relevant.

According to our study, there are more malformations in IVF group compared with non IVF group. On the other hand seems that those malformations are not related with BW, GA and complications of prematurity.

We conclude that although our retrospective study showed statistically significant malformations on IVF (5.8%) compared to non-IVF group, we cannot conclude that is more frequent, because the result is not too much different from the general newborn population malformation rate (3 - 5%).

***Keywords:*** *In Vitro Fertilization; Malformations*

## Background

*In vitro* fertilization (IVF) refers to a procedure designed to overcome infertility and produce a pregnancy as a direct result of the intervention.

In general, the ovaries are stimulated by a combination of fertility medications and then one or more oocyte(s) are aspirated from ovarian follicles. These are fertilized in the laboratory ("*in vitro*"), after which, one or more embryo(s) are transferred into the uterine cavity (Figure 1).

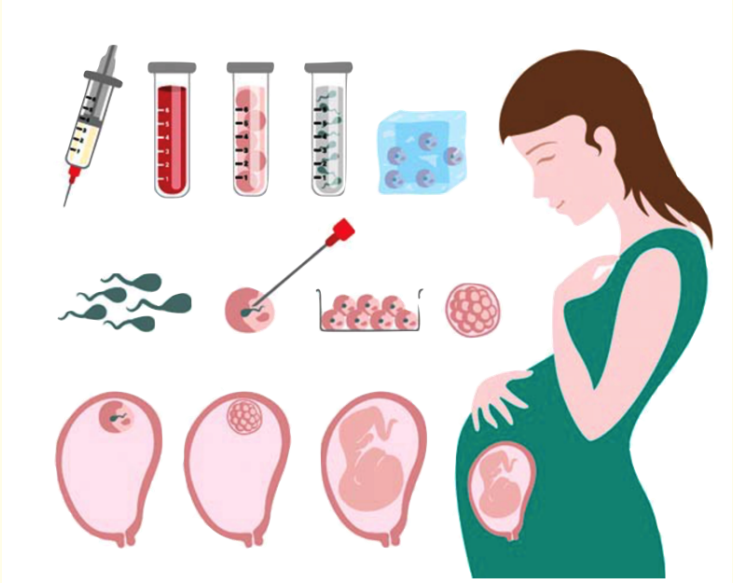

***Figure 1:*** *IVF steps.*

## Aim of the Study

The purpose of the study was to see how many newborns showed malformations, compared with other non - IVF group and related this finding with the gestational age, birth weight and common complications of prematurely like respiratory distress syndrome (RDS) and necrotizing enterocolitis (NEC).

## Materials

We reviewed all newborns admitted in NICU during a period of five years (2015 - 2019). There was a total 2875 cases.

At the same period born 422 IVF babies. Of these, 68 were admitted at NICU.

## Methods

This was a retrospectively reviewed.

We compared the IVF cases (68) with the non IVF cases (2807).

We analyzed the two groups and compared the distribution of gestational age, birth body weight, hospitalization days, admission rate, short-term complications (RDS and NEC), mortality and malformations.

We used Mann-Whitney test and chi-square test (when 1 < the expected cell frequencies < 5, use Yates correction) to calculate P value. When P value < 0.05, it is statistically significant.

## Results

The gestational age (GA) of IVF newborns admitted in NICU was mainly between 32-36W+6 and their birth weight (BW) was between 1.5 and 2.5 kg (Figure 2 and 3).

| GA | 22-27W+6 | 28-31W+6 | 32-36W+6 | ≥37W | |
|---|---|---|---|---|---|
| NO.(%) | 3(4.4%) | 6(8.8%) | 41(60.3%) | 18(26.5%) | 68 |

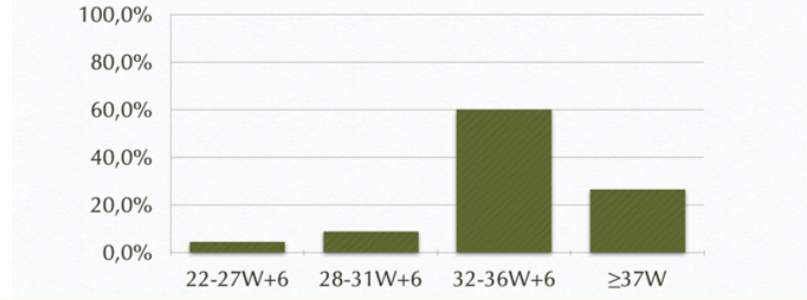


***Figure 2:*** *Gestational age distribution of IVF cases in the NICU.*

| BBW | <1kg | 1≤BBW<1.5kg | 1.5≤BBW<2.5kg | ≥2.5kg | |
|---|---|---|---|---|---|
| NO.(%) | 3(4.4%) | 5(7.4%) | 43(63.2%) | 17(25%) | 68 |

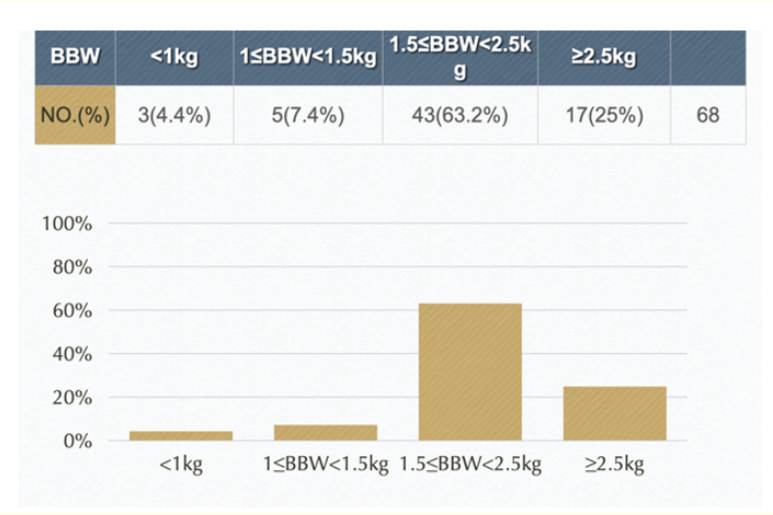


***Figure 3:*** *Birth body weight distribution of IVF cases in the NICU.*

Four of the IVF newborns admitted to NICU had congenital malformations (The rate was 5.8%) compared with zero cases in non IVF group. This result was statistically significant. The malformations detected were: duodenal atresia, anal atresia, cleft lip and palate, ventricular septal defect (Figure 4).

| Malfomation | NO. |
|---|---|
| Cleft lip and palate | 1 |
| Duodenal atrsia | 1 |
| Anal atresia | 1 |
| VSD | 1 |

***Figure 4:*** *Malformations of IVF cases in the NICU.*

The incidence of prematurity, low birth body weight, short term complications (HMD, NEC) and long hospital stays in IVF group is higher than non-IVF group and are also statistically significant (Figure 5-7).

IVF group V.S Non-IVF group in gestation age

| GA | <=37W | >37W | Total | |
|---|---|---|---|---|
| IVF | 54 | 14 | 68 | $P_1$=79.4% |
| Non-IVF | 640 | 2167 | 2807 | $P_2$=22.8% |
| | | | 2875 | P<0.05 |

IVF group V.S Non-IVF group in birth body weight

| BBW | <2.5kg | ≥2.5kg | Total | |
|---|---|---|---|---|
| IVF | 51 | 17 | 68 | $P_1$=75% |
| Non-IVF | 563 | 2244 | 2807 | $P_2$=20% |
| | | | 2875 | P<0.05 |

***Figure 5:*** *Compared study between IVF and non-IVF group (GA and BW).*

Admission date

| Date | Average±SD | |
|---|---|---|
| IVF | 17±19.52 | P <0.01 |
| Non-IVF | 7±0.55 | |

Admission rate

| | In UCERN | Non-UCERN | Total | |
|---|---|---|---|---|
| IVF | 68 | 354 | 422 | $P_1$=16.1% |
| Non-IVF | 2807 | 13214 | 16021 | $P_2$=17.5% |
| | 2875 | 13568 | 16443 | P>0.05 |

***Figure 6:*** *Compared study between IVF and non-IVF group (Admission).*

Complication of RDS

| | RDS | Non-RDS | Total | |
|---|---|---|---|---|
| IVF | 21 | 47 | 68 | $P_1$=30.4% |
| Non-IVF | 133 | 2674 | 2807 | $P_2$=4.7% |
| | 154 | 2721 | 2875 | P<0.05 |

Complication of NEC

| | NEC | Non-NEC | Total | |
|---|---|---|---|---|
| IVF | 4 | 64 | 68 | $P_1$= 5.9% |
| Non-IVF | 42 | 2765 | 2807 | $P_2$= 1.4% |
| | 46 | 2829 | 2875 | P<0.05 |

***Figure 7:*** *Short complications.*

The mortality rate of both groups was statistically not relevant (Figure 8).

| | Death | Survival | Total | |
|---|---|---|---|---|
| IVF | 3 | 65 | 68 | $P_1$=4.4% |
| Non-IVF | 41 | 2766 | 2807 | $P_2$=1.5% |
| | | | 2875 | P>0.05 |

***Figure 8:*** *Mortality rate.*

## Discussion and Conclusion

IVF is very important for the couple that don't have the possibility to have a baby and want so much to be parents after some period of trying naturally.

This technique is not indicated in all situations.

What are the indications for IVF?

Fertility issues:

- Tubal factor
- Severe male factor infertility
- Diminished ovarian reserve
- All other causes of infertility, after failing treatment with less invasive therapies
- Ovarian failure
- Uterine factor.

Others:

- Sex selection
- Preimplantation genetic diagnosis
- Prevention of mitochondrial disorders
- Potential correction of germline mutations
- Genetic parenthood for same-sex couples.

There are no contraindications to the procedure of IVF bur some disease showed more risks. The diseases are: Marfan syndrome, heart failure, Eisenmenger syndrome, severe valvular stenosis, pulmonary hypertension, or coarctation of the aorta.

In these cases need to use IVF with oocyte aspiration, fertilization with their partner's sperm, but the embryos will be transferred to a gestational carrier.

We know that 20% of gestations with malformation fetus will end in spontaneous abortion.

The rest 80% will born death or alive with some congenital anomalies, resulting in 3 - 5% of malformations at birth. This congenital malformations will result in 20% of deaths of postnatal period.

The most common cause of congenital defects occurred in the first three months of pregnancy. Genetic, infectious, nutritional and environment are the main causes.

Our preliminary study showed that seems there are more malformations in IVF group compared with non IVF group. This finding was statistically significant.

Those malformations are not related with BW, GA and complications of prematurity.

Although our study showed that statistically the result between IVF and non-IVF group was significantly, if we compared to the common 3 - 5% of malformations in the newborn population, the difference is 0,8%.

In this study we didn't evaluate the maternal age of the IVF group and we know that this will increase the malformation and chromosome disorder, if the maternal age is advance. Most situations, the couple decide to do the IVF after years of waiting to have a baby by natural way. This variant (maternal age) can be important to correlate with the findings of those four cases with malformations and was not study in this review. The reason for this absence data, was because of lack of information about the mother age at the newborn file.

We conclude that although our retrospective study showed statistically significant malformations on IVF (5.8%) compared to non-IVF group, we cannot conclude that is more frequent, because the result is not too much different from the general newborn population malformation rate (3 - 5%) [1-7].

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