



Medically Assisted Procreation: its risk in the maternal-fetal and neonatal pathology

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ABSTRACT

The increase of the Medically Assisted Procreation is due to the effort that the research has made to improve the techniques, but its effect on the maternal outcome and neonatal outcome has not been fully studied. Therefore, our study has focussed on a population of pregnant women hospitalised in the obstetrical pathology unit at the S. Giovanni Calibita Fatebenefratelli hospital in Rome in the year 2013.

First of all, we have made a distinction between the women who have undergone an assisted reproductive technology (ART) and those in a spontaneous pregnancy and, successively, for each of them, we have evaluated the clinical history, the reason for admission, the course of the pregnancy, the outcome of childbirth and the clinical condition of the newborn. This work emphasises the common profile of the woman who underwent ART: multiple pregnancy, advanced maternal age, chronic diseases such as hypertension, hospitalisation for cervical incompetence and threats of preterm birth, preterm birth, caesarean section, premature babies with necessity of a recovery in intensive and sub intensive care, increased hospitalisation of mother and infant. In the future it becomes necessary to regulate the ART by using these results increasingly, both to select the patients and to choose the methods of prophylaxis and prevention of complications.

Keywords: medically assisted procreation; maternal outcome; neonatal outcome; assisted reproductive technology; multiple pregnancy; advanced maternal age; preterm birth; premature babies.

SOMMARIO

L'incremento delle procedure di Procreazione Medicalmente Assistita (PMA) è dovuto allo sforzo che la ricerca ha fatto per migliorarne le tecniche, pur non valutandone gli effetti sull'outcome materno e neonatale. A riguardo il nostro studio ha preso in esame una popolazione di donne gravide che sono state ricoverate nel reparto di patologia ostetrica dell'ospedale Fatebenefratelli S. Giovanni Calibita Isola Tiberina (Rm) nel corso dell'anno 2013.

Per prima cosa si è suddivisa la popolazione rispettivamente in donne che si sono sottoposte a PMA e donne che hanno concepito spontaneamente. In seguito, per ognuna, sono stati valutati i seguenti elementi: la storia clinica, il motivo del ricovero, il decorso della gravidanza, gli esiti del parto e le condizioni cliniche del nascituro.

Lo studio ha messo in evidenza caratteristiche comuni e ricorrenti nelle donne che si sono sottoposte a PMA: prevalenza di gravidanza gemellare, età materna avanzata, patologie croniche materne come l'ipertensione, ricoveri per incompetenza cervicale e minacce di parto pretermine, bambini nati pretermine, taglio cesareo, neonati prematuri con necessità di ricoveri in terapia intensiva e sub-intensiva, aumento delle degenze della madre e del neonato. Pertanto in futuro risulta necessario regolamentare la PMA utilizzando maggiormente questi risultati sia per selezionare le pazienti sia per scegliere metodiche di profilassi e prevenzione delle complicanze.

INTRODUCTION

At all ages and in all societies infertility has constituted a major health problem, mainly related to the negative effects that longevity and environmental pollution have on the fertility of couples⁽¹⁾. As a result, the demand for medical care is growing accordingly, as demonstrated by the wide variety of supporting treatments to alleviate infertility, such as an improvement of the in vitro fertilization technique and a growing availability of oocyte donation techniques⁽²⁾. The medically assisted procreation has indeed become available to a wider population allowing for greater knowledge about both its techniques and the problem of infertility itself. The increase of "artificial" pregnancies go on over time soliciting a series of important repercussions from the clinical point of view and for what concerns the healthcare and the clinical expenses. The factors that can determine a favourable or unfavourable evolution of the gestation, independent from the technical ability of the biologists in the reproduction, are the increased maternal age⁽³⁾, the gestational ability of a less elastic uterus⁽⁴⁾, the frequency of multiple pregnancies⁽⁵⁾, the starting organic conditions of the mother are among. To this day, it is therefore necessary to carefully observe the quality of the pregnancies obtained via the assisted reproductive technology (ART) referring to the maternal-fetal and neonatal outcome. So we have conducted a perspectival study during a calendar year evaluating the effect of the ART recoveries against non ART recoveries in the obstetrician pathology division of the Fatebenefratelli hospital in Rome. We have classified the patients progressively hospitalised for problems developed during their pregnancy, taking into consideration the main diagnosis that had prompted their hospitalisation and following the therapeutic process and neonatal outcomes.

SUBJECTS AND METHODS

The experimental study was conducted in the obstetrician pathology division of the S. Giovanni Calibita Fatebenefratelli hospital in Rome, in agreement with the Tor Vergata University of Rome. In the period January-December 2013, 353 women were selected after being hospitalised due to a pathology arisen during their pregnancy. Each woman has been hospitalised at least once during the time span. Patients have been followed longitudinally along pregnancy and their maternal and neonatal outcome recorded for final analysis. Specifically, the Record book has allowed us to

derive a nosographic number of the patients, from which we have traced telematically their own Personal Codes and, as a consequence, the clinical records each of them had collected, reaching a total of about 549 folders consulted. Moreover, through the folder of the woman giving birth, we have traced the Personal Code and the medical record of the newborn, from which we have derived data for a total of about 306 pediatric folders consulted, taking into account that for some children it was possible to obtain information only from the "Born" paper Record books, stored in the Neonatology hospital.

The elaboration of the results was based upon the separation of two classes of the population, 70 of which have undergone the ART (19,83%) and 283 have not undergone the ART (80,27%). Starting from this division (Patients ART and Patients non ART) the Neonatal Populations were derived: a total of 344 babies born alive, 94 of which born from the Pts ART (27,32%) and 250 born from Pts non ART (72,68%). For each population a study was drafted taking into consideration the several variables that could be analysed. For what concerns the maternal population, the following data were taken into account: maternal age; hypertensive diseases; threat of preterm birth; gestational age; type of pregnancy; number of hospitalisations for patient and total days of hospitalisation; mode of delivery. For the neonatal population: neonatal anthropometric evaluation; birth pathologies; internal transfers or transfers to other hospitals; days of hospitalisation of infants. Each subgroup was then uniformed with quantitative measures accurately calculated and represented both by the absolute values and by measures proportional to the total percentage of the reference populations and/or the percentage of the total of each qualitative variable.

RESULTS

From our study were derived results divided by maternal population, neonatal population and, finally, public health considerations regarding both populations.

Maternal population

Maternal age was divided into intervals of five years, except for the age groups of less than twenty years. From this we have obtained the descriptive statistics: those women who had chosen ART have an average age of 38,68 and the modal class between 35 and 39 years old (30%) is the one with a largest number of pregnant women. The non ART women, on the other hand, have an average

of 33,38 years and the modal class in which the highest number of pregnancies concentrates is between 30 and 34 years old (36,04%).

Table 1.
Division of the maternal age-by-age groups and the maternal population into patients who have or not undergone ART.

| Maternal Age | < 20 yo | 20 - 24 yo | 25 - 29 yo | 30 - 34 yo | 35 - 39 yo | 40 - 44 yo | 45 - 49 yo | 50 - 55 yo |
|----------------------|---------|------------|------------|------------|------------|------------|------------|------------|
| Pts ART | 0 | 2 | 4 | 11 | 21 | 17 | 13 | 2 |
| % Pts ART | 0.00% | 2.86% | 5.71% | 15.71% | 30.00% | 24.29% | 18.57% | 2.86% |
| Pts non ART | 3 | 15 | 42 | 102 | 86 | 33 | 2 | 0 |
| % Pts non ART | 1.06% | 5.30% | 14.84% | 36.04% | 30.39% | 11.66% | 0.71% | 0.00% |
| Total Pts | 3 | 17 | 46 | 113 | 107 | 50 | 15 | 2 |
| Total % | 1.06% | 8.16% | 20.55% | 51.75% | 60.39% | 35.95 | 19.28% | 2.86% |

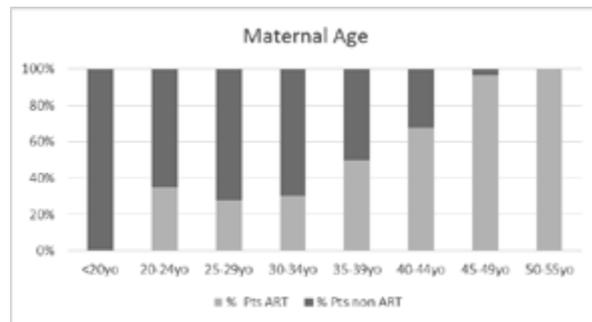


Figure 1.
Descriptive histogram of the maternal age groups in which the highest distribution of the Pts ART is evidenced in the groups of more advanced age, mostly 35 years or older, compared with the Pts non ART that are distributed more around 34 years of age or younger.

By subdividing the pregnancy into single and multiple, hence bigeminal and trigeminal, we derive that 52,86% of the pregnancies of the Pts ART are unique, while 47,14% are multiple (40% bigeminal and 7,14% trigeminal). Among the women who have not undergone ART, on the contrary, the percentages vary considerably: 92,58% of the pregnancies are single, while 7,42% are multiple (7,07% bigeminal and 0,35% trigeminal). If we observe the same data within the total population of patients, there is an absolute prevalence of the single pregnancy. In the Pts non ART, that is 74,22% against the 10,48% of the Pts ART and a clear predominance of the multiple pregnancy in the Pts ART, that is 9,35% (7,93% B; 1,42% T), compared to the 5,95% (5,67% B; 0,28% T) in the Pts non ART.

Table 2.
Data collection per kind of pregnancy on the population of patients who have undergone ART or not have.

| | Pregnancy | | | Total |
|--------------------|-----------|-----------|------------|-------------|
| | Single | Multiple | | |
| | | Bigeminal | Trigeminal | |
| Pts ART | 52.86% | 40% | 7.14% | 100.00%=70 |
| | 10.48% | 7.93% | 1.42% | 100.00%=353 |
| Pts non ART | 92.58% | 7.07% | 0.35% | 100.00%=283 |
| | 74.22% | 5.67% | 0.28% | 100.00%=353 |

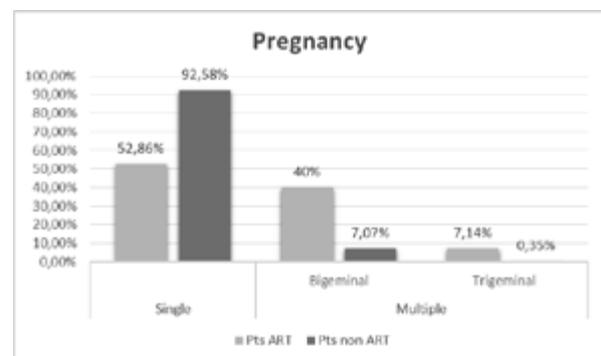


Figure 2.
Distribution of each maternal population, which is Pts ART and Pts non ART, within the subdivision of the pregnancy into single and multiple, in turn bigeminal and trigeminal.

In this study we have observed the pathological conditions occurred during these pregnancies, more precisely we have focussed on the hypertension, both chronic and gestational, in the 20% of the Pts ART compared to the 10,6% of the Pts non ART.

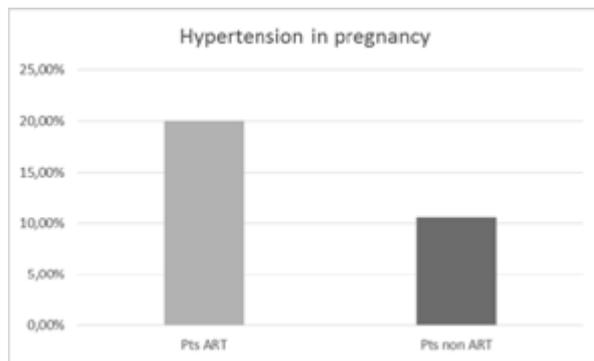


Figure 3.

In the evaluation of the pathological conditions of the mother we have taken into account the hypertensive disease. The results are referred to the following pathologies: chronic and gestational hypertension, preeclampsia, eclampsia and HELLP. The distribution of the hypertensive pathology evidences its higher impact in the group of the Pts ART.

In the same way, we have considered the cases of threatened preterm delivery (TPT), of cervical incompetence (CI) and of premature membranes rupture (PROM) and preterm PROM (pPROM).

On the whole, we can see how the threatened of preterm births is more frequent in the women who have a spontaneous pregnancy (35,69% in Pts non ART; 30% in Pts ART). But, if we consider their highest number, among the Pts ART we find a higher prevalence of CI and pPROM, that is 34,28% in the first and 10% in the latter, compared to 16,96% in the first and 5,65% in the latter in the case of the Pts non ART. On the other hand, among the Pts non ART there is a higher prevalence of PROM, that is 10,25% compared to 8,57% in the Pts ART.

Table 3.

In the maternal population were collected data on those cases where the pathology arises during the pregnancy. We have taken into account, for both the Pts ART and non ART, threatened preterm delivery (TPT), cervical incompetence (CI), premature membranes rupture (PROM) and preterm PROM (pPROM).

| | TPT | CI | PROM | pPROM | Total |
|--------------------|--------|--------|--------|-------|-------------|
| Pts ART | 30% | 34.28% | 8.57% | 10% | 100.00%=70 |
| Pts non ART | 35.69% | 16.96% | 10.25% | 5.65% | 100.00%=283 |

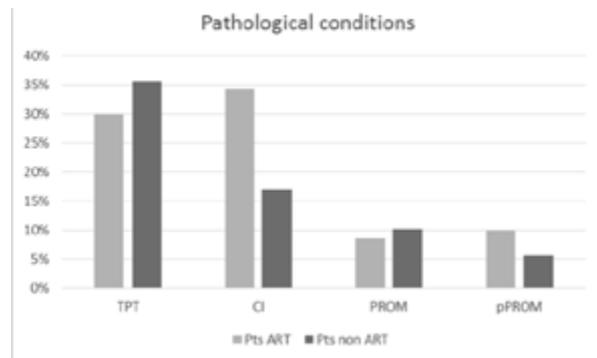


Figure 4.

Graphic representation of the results presented in the table. Notice the high frequency of preterm birth threats both in the Pts ART and in the non ART. On the other hand, cervical incompetence and premature PROM are evidently more frequent among the Pts ART.

The gestational age was subdivided into intervals, mainly respecting the concepts of term pregnancy and pre-term pregnancy. The gestational age of the Pts ART was distributed among 62,5%, where we have it between the 32nd and 36th week +6 days and for a 23,21% over the 37th week. Viceversa, the distribution of the gestational period in the Pts non ART: 53,95% of them has a term pregnancy, while 29,82% has a pregnancy between the 32nd and 36th week +6 days.

Table 4.

Subdivision of the gestational age of the patients, both ART and non ART, in intervals that consider the term and pre-term pregnancy.

| | Gestational Age | | | | | Total |
|--------------------|-----------------|--------------|--------------|--------|-------|-------------|
| | 24 - 27w+6dd | 28 - 31w+6dd | 32 - 36w+6dd | Term | >41w | |
| Pts ART | 1.79% | 12.50% | 62.5% | 23.21% | 0.00% | 100.00%=57 |
| Pts non ART | 3.95% | 8.77% | 29.82% | 53.95% | 3.51% | 100.00%=228 |

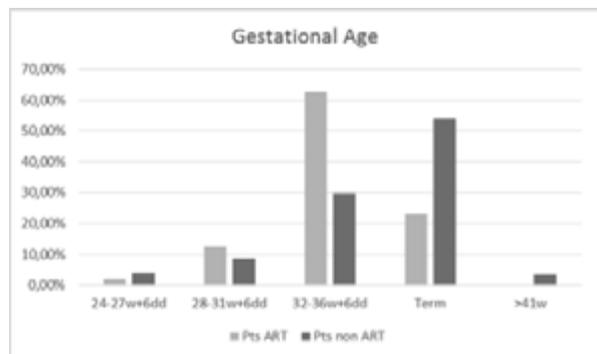


Figure 5.

Representation of the distribution of the patients, ART and non ART, in intervals of gestational age. The pregnancies in the Pts ART are distributed mainly in 36 weeks +6 days, the pregnancies of the Pts non ART go to term.

Completed pregnancies were divided per type of delivery: spontaneous, operative and caesarean section. Overall, the caesarean prevails and it is configured in 85,96% of deliveries in the Pts ART and in 63,60% of the Pts non ART.

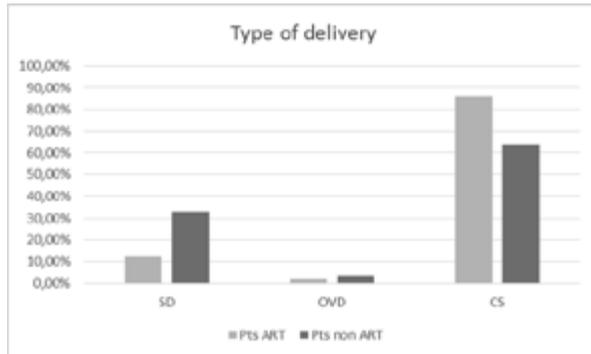


Figure 6. Graphic distribution of the type of delivery, that is spontaneous or vaginal operative, and caesarean section. Percentage values of the type of delivery made by the patients and considered both with respect to the total in each group, Pts ART or Pts non ART, and to the total of the maternal population. In both populations, Pts ART and Pts non ART, the caesarean prevails.

Neonatal population

First of all, we have considered if a newborn is or not appropriate for the gestational age by using the new Italian Neonatal Anthropometric Papers, realised with participation from 34 Neonatology centres within the Italian Neonatal Study (INeS). The newborn have then been classified in small for gestational age (SGA), appropriate for gestational age (AGA) or large for gestational age (LGA). The results have shown that the infants are mainly distributed in the AGA class in both populations (80,35% for those born from ART; 87,20% for those not born from ART), but there are differences in the other two classes SGA and LGA. Those born from ART have a higher distribution within the SGA class (17,02% on a total of children born from ART), compared to those not born from ART (9,60% on a total of children not born from ART). On the contrary, those not born from ART have a higher distribution within the LGA class 3,20% idem) compared to those born from ART (2,13% idem).

Table 5. The relationship between gestational age and birth weight of the infants allow us to distribute them into small for gestational age (SGA), appropriate for gestational age (AGA) and large for gestational age (LGA). To do this we have made use of the new Italian Neonatal Anthropometric Papers.

| | Classes of the Gestational Age | | | Total |
|-------------------|--------------------------------|----------------------------|------------------------|-------------|
| | SGA (<10th percentile) | AGA (10th-90th percentile) | LGA (>90th percentile) | |
| Born from ART | 17.02% | 80.85% | 2.13% | 100.00%=94 |
| Not born from ART | 9.60% | 87.20% | 3.20% | 100.00%=250 |

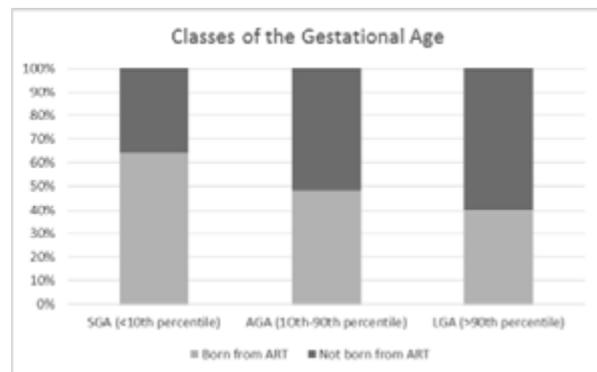


Figure 7. The newborn appropriate for the gestational age represent the majority of babies born from ART and non ART. The small newborn for gestational age are of a higher number when born from ART. The large newborn for gestational age are of a higher number when not born from ART.

The consultation of the clinical records of the newborn babies has showed various pathological cases, according to which the newborn have been classified into healthy and sick, also taking into account the prematurity and the respiratory distress syndrome. The children born ill from ART represent the 75,53% of this population, 61,70% of which is premature and 29,79% has got RDS, while the healthy are just 24,47%. The children not born from ART present a higher percentage of health than the previous ones, that is 52,80% and, among the sick ones, not born from ART, the 31,20% is premature and the 19,20% has got RDS.

Table 6.

In the evaluation of the pathological conditions of the newborn we have taken into account eight subgroups: prematurity (Pm); respiratory distress syndrome (RDS); malformations (M); jaundice (J); anemia (A); hemorrhage (H); coagulopathy (C); infections (Inf).

| | Sick born | | | | | | | | Healthy born |
|-------------------|-----------|--------|--------|--------|-------|-------|-------|-------|--------------|
| | Pm | RDS | M | J | A | H | C | Inf | |
| Born from ART | 71.28% | 29.79% | 20.21% | 11.70% | 6.38% | 4.25% | 0.00% | 5.32% | 24.47% |
| Not born from ART | 31.20% | 19.20% | 21.60% | 16.80% | 7.60% | 4.80% | 4.80% | 6.40% | 52.80% |

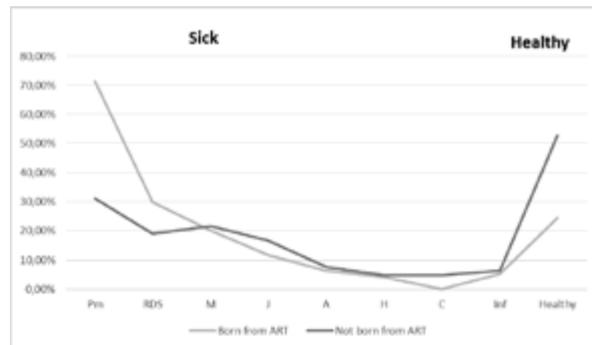


Figure 8.

The graphical representation distributes the subgroups of the pathologies and highlights the predominance of sick infants, premature (Pm) and with respiratory distress syndrome (RDS), among those born from ART.

Moreover, the children born with problems during birth or during the pregnancy have been moved into other divisions in the same hospital, such as intensive and sub-intensive therapy, and in other hospitals, due to saturation problems or because of in need of paediatric surgery. Being the total 344, 142 of them has required neonatologic assistance (41,28% of the total of the newborn babies) and of these 66 were born via ART (19,19% on a total of the newborn), while 76 were not born from ART (22,09% of the total of the newborn). In particular, those born from ART are mainly distributed in the II level functional units of the hospital object of the study (17,61% in Sub-TIN and 13,38% in TIN). While, those not born from ART are mostly concentrated in the I level functional unit in the same hospital (26,06% in the neonatal pathology division) and another good part were transferred to another hospital (14,08%).

Table 7.

Distribution of the ill children within the intensive therapy unit (ITU), sub-intensive therapy unit (Sub-ITU), neonatal pathology unit (NPU) or other hospitals.

| | Transfer Distribution | | | | Total |
|-------------------|-----------------------|---------|--------|----------------|-------------|
| | ITU | Sub-ITU | NPU | Other hospital | |
| Born from ART | 13.38% | 17.61% | 11.27% | 4.22% | 100.00%=142 |
| Not born from ART | 6.34% | 7.04% | 26.06% | 14.08% | 100.00%=142 |

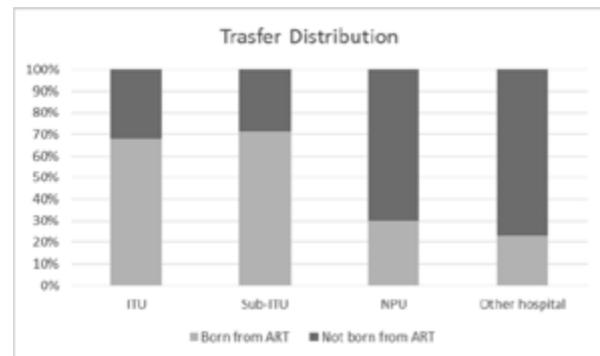


Figure 9.

Those born from ART are distributed mostly in the intensive (ITU) and sub-intensive therapy units (Sub-ITU). Those not born from ART are mainly distributed in the neonatal pathology unit (NPU) or are transferred to another hospital.

Considerations of Public Health

Through the medical records, we were able to calculate the days of hospitalisation of both the mothers and the infants. The Pts ART have a lower number of hospitalisation compared to the Pts non ART but, at the same time, the days of hospitalisation of the former are greater than those of the other. The average of admissions and days of hospitalisation in the Pts ART is 10,09, compared to 9,54 in the Pts non ART, with a history of hospitalisation higher than 87 days in the first group, compared to 69 days in the second group.

Table 8.

Collection of the hospitalisation's number and of the total days of hospitalisation for the patients, both ART and non ART. Resulting evaluation of the average number of days and number of hospitalisations.

| | Number of hospitalisations | Total days of hospitalisations | Average Days / Hospitalisation |
|-------------|----------------------------|--------------------------------|--------------------------------|
| Pts ART | 97 | 1561 | 16.09 |
| Pts non ART | 456 | 4350 | 9.54 |
| Total | 553 | 5911 | 10.69 |

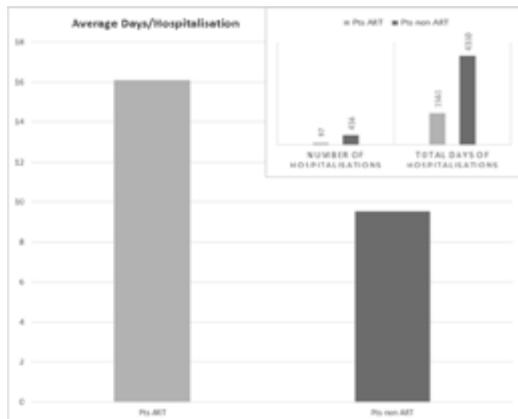


Figure 10. Graphic representation of the tabulated values. As we can see, the Pts ART have a lower number of hospitalisations compared to the Pts non ART, but the hospitalisation per se has a duration in terms of days higher than the patients who have not undergone ART.

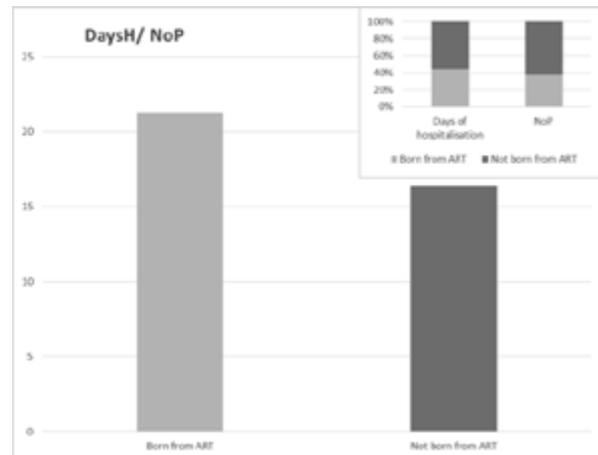


Figure 11. Graphic representation of the tabulated values. We can see how, starting from the days of hospitalisation and the number of patients, the children born from ART have on average a higher number of days of hospitalisation compared to those not born from ART.

In the population born from ART, constituted by 94 components, we have 1541 days of recovery, mainly collected by those born from multiple pregnancies. Just think that there are 5/3 born in this population and the days of hospitalisation accumulated by them only is 149. Among those born not from ART, 250 babies, we have 1933 days of recovery, mainly derived from the firstborn (more numerous of the first population). The description of the neonatal wards can be summed up in the following equations:

- 71 NoP: 1541 days = 1 NoP: 21,27 days (no.1)
- 118 NoP :1933 days = 1 NoP: 16,38 days (no.2)

In the equation no.1 is evidenced not only the number of patients (NoP), born from ART, 71 of a total of 94 children, but also that each one of them has on average 21,27 days of hospitalisation.

In the equation no.2 is on the contrary evidenced the number of patients, born not from ART, that is 118 of a total of 250 children, and each one of them has an average of 16,38 days of hospitalisation.

Table 9. Collection of the total days of hospitalisation for children and their number (NoP), both born from ART and not. Resulting evaluation of the average days of hospitalisation and number of patients.

| | Days of hospitalisations | NoP | DaysH/ NoP |
|-------------------|--------------------------|-----|------------|
| Born from ART | 1541 | 71 | 21.27 |
| Not born from ART | 1933 | 118 | 16.38 |

DISCUSSION

In Italy, from an ethical, legal and medical point of view, the Medically Assisted Procreation is a topic more relevant than ever for the increase in the number of women who undergo the insemination techniques. This stems especially from the increase in pregnancies for women over forty years of age in western countries, due to economic and social reasons related to study and career choices.

In our research the women of advanced age represent the majority of those who underwent the medically assisted procreation, while women with spontaneous pregnancies slightly exceed the threshold of forty years of age. Given that the index of fertility diminishes with the increasing age of the woman, the postponement of the pregnancy has become a problem in the reproductive health and this could explain the consistent use of the procreation in these age groups and, recently, this trend has been fostered by the development of the egg donation techniques, that offer higher chances of success for those women who carry them out in menopausal and postmenopausal periods. However, we should not create an axiom between the state of sub-fertility in a woman of advanced age and the use of the medically assisted procreation, because an increased maternal age can also increase complications during pregnancy⁽⁶⁾.

Procreation has mainly had, in the last few years, an important role in increasing the incidence of multiple pregnancies. The population observed in the course of this study facilitates the emergence of a high percentage of these, among the Pts ART,

in which the 50% is of a twin kind, and this result highlights the association between the number of twin pregnancies and the advanced age of the patients. We, in fact, know that the age factor reduces the efficiency of the medically assisted procreative technique and, as a consequence, induces to a transfer of at least three embryos in the uterus to guarantee its success⁽⁷⁾. The complications associated to multiple pregnancies and their cost have caused a reshaping of this trend through the concept of the transfer of a single embryo.

Yet, we shall not lose sight of the reasons for the recovery in the obstetrician pathology that are often connected to very serious complications and are not made irrelevant by the choice of a non-spontaneous pregnancy. We shall consider, for example, the chapter on the hypertensive disease that is present not only in the 12,47% of the population under study, but especially among the patients who have undergone an assisted procreation. The women belonging to this group are older than 35 years, however, as we have seen, they are more inclined to an increase of the risk factors, among which chronic diseases and complications for the newborn, such as preterm birth (gestational age <32 weeks), low weight at birth (weight at birth <2500 g) and perinatal death.

A more advanced age implicates a minor predisposition of the body of the pregnant woman to welcome the unborn and carry out the pregnancy, due to factors such as the reduction in the elasticity of the tissues that could for instance cause cervical incompetence and, as a consequence, a preterm birth. Indeed, among the population under study as a whole the cases of recovery for threats of preterm delivery are very frequent, but among the Pts ART the cases of cervical incompetence are more frequent.

It is not by chance that in the sample of Pts ART the majority of women carries out their pregnancy between "32 weeks + 0 days", so that their children are born preterm. Prematurity is strictly related to the history of the pregnancy of the woman, for reasons like the very young age or the advanced maternal age, the too short time lapses between pregnancies, a low BMI and uterine over distension because of multiple pregnancies that increases by ten times the risk of preterm birth compared to single pregnancies. From the neonatal point of view, prematurity encompasses the most part of the pathological events encountered in the neonatal population, of which 3/4 were born from ART, and it is related to the clinical history of these children who show a low weight at

birth, RDS, malformations, bronchopulmonary dysplasia, anemia, jaundice and infections. But the advanced age affects the preterm births, also conditions at risk for women in this period of their life, such as NCDs (hypertension and diabetes) that, presenting themselves as threats during the pregnancy, can induce women to choose between the chance of an induced preterm birth or the possibility of an urgent delivery.

All this is exacerbated by the fact that the Pts ART, as we have seen, have with a higher frequency a multiple pregnancy and, as a consequence, to sustain the growth of a uterus containing more foetuses reduces its chances of growth compared to a single foetus and it induces earlier break of the membranes due to a mechanical stress of the wall because of a higher distension of the uterus in a multiple pregnancy. The data regarding the high prevalence of premature babies born from ART explains their higher hospitalisation and the need they have of a more proper healthcare. These newborn are especially hospitalised in Sub-TIN and TIN, so there is an obvious difficulty in the neo family that cannot go back home "with the baby in their arms". This difficulty is even worse when the baby is transferred to other hospitals because of the saturation of beds or when the babies born from the same multiple pregnancy are transferred in different divisions for the same reason described above.

The organisation of the services thus represents an overall area of improvement and a greater consistency between obstetrical levels remains a desirable objective and something to persevere with an interdisciplinary effort especially for what concerns the prenatal diagnosis, surgical services and neonatal intensive therapy services.

It thus appears clear from the data presented how the incidence in the medically assisted procreation in the activities of the obstetrical pathology division can be characterised by a lower number of patients compared to those with spontaneous conception, but with a duration in the hospitalisation and a relationship between the days and the number of hospitalisations higher than the patients who have given birth spontaneously.

There has also been a clear rise, in this group, of prematurity, maternal pathologies during the pregnancy and all the neonatal complications. In the healthcare the cost of hospitalisation increases exponentially with its duration that is clinically related to the need for health care on the part of the woman.

It was relevant to note how it is the Pts ART themselves that accumulate more days in hospital, while the Pts non ART accumulate a higher number of hospitalisations. These results expose a conduct that presents more certainty in knowing the risks connected with pregnancies obtained through ART, since most of the women who undergo ART have risk factors already known, such as advanced age and multiple pregnancies. Moreover, if we consider that in the obstetrical pathology divisions the number of beds is limited, the 20% of Pts ART hospitalised at the San Giovanni Calibita Fatebenefratelli hospital in Rome becomes a conspicuous percentage if related to their long-term care compared to a woman with spontaneous pregnancy in the same division. It is easy to imagine how this affects the health expenditure and the availability of beds.

The same can be said about the neonatal sphere, where notwithstanding the undeniable progress made and the success achieved in the maternal-neonatal area, the prevalence of the preterm births does not show any sign towards a reduction of the time, also due to the emergence of the new gravid conditions described above. In our job the number of preterm births and the number of hospitalisations are higher than the pregnancies due to medically assisted procreation. Is we

estimate the days accumulated by each newborn baby, considering the fact that he/she is an only child or first-born, second-born and/or third-born in a multiple pregnancy, the third-born are those who accumulate more days.

In summary, the largest number of multiple pregnancies among the women who have undergone ART (triplet deliveries in particular) and the largest number of preterm births give account of the conspicuous duration of the neonatal hospitalisation. The costs are high on this front as well, not just considering the direct health expenses, but also for the healthcare commitment, both global and at a distance.

It is therefore important to have a regulation of the Medically Assisted Procreation that can allow for a selection of the patients to be subjected to this treatment, taking into account the repercussions there can be upon the national healthcare system. As a matter of fact, a methodology applied irrationally and with no selective criteria generates consequences on the cost of hospitalisation and on the health of both patients and newborn babies.

In the future a greater use of these results will allow us to evaluate the efficacy in the selection of the patients, the possible methods of prophylaxis and the prevention of the complications.

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