Biochemical Infertility Among Prospective Oocytes' Donors at the University of Ilorin Teaching Hospital Assisted Reproductive Unit, Nigeria.

[1,3]S.A Biliaminu, [1]I.M AbdulAzeez, [1]A.A Akande, [1]A.B Okesina, [2,3]A.W.O Olatinwo, [2,3]L.O Omokanye,

[1,3]Department of Chemical Pathology and Immunology, [2]Department of Obstetrics and Gynaecology, [3]Assisted Reproductive Therapy Unit, University of Ilorin, Ilorin, Kwara State, Nigeria.

Abstract

With the advent of Assisted Reproduction, egg donation now makes pregnancy possible for women who might not otherwise be able to get pregnant using their own eggs thus warranting the assistance of oocytes' donors. Prospective oocytes' donors are biochemically screened apart from genetic, physical and psychosocial screening to ensure their suitability. The aim of this study was therefore to evaluate prevalence and pattern of biochemical abnormalities, even in third party clients at our Assisted Reproductive Therapy Unit.

Forty-eight prospective oocytes' donors who presented between June 2012 and December 2016 at the University of Ilorin Teaching Hospital Assisted Reproductive Unit, Nigeria for possible recruitment as third party subjects for assisted reproduction procedures had their fasting blood samples collected for fertility profile assay. This was done as part of their routine laboratory tests to ascertain their suitability for the procedures. The results of the fertility profile hormonal assays were statistically analyzed.

The mean age for all the prospective oocytes' donors in this study was 22.63±2.28 years, the youngest of them being 19 while the oldest was 30 years old. Twenty-one (43.17%) of the prospective oocytes' donors with mean age of 21.95±2.25 years had normogonadotrophic normogonadism (biochemically normal) while twenty-seven (56.83%) of them with mean age of 23.6±2.4 years had either one form or another biochemical abnormality. Nine (18.75%) of them with mean age of 22.78±2.17 years were accidentally found to have hyperprolactinaemia, 14 (29.17%) with mean age of 22.79±1.63 years had polycystic ovarian syndrome while 4(8.33%) of them had hypergonadotrophism (premature ovarian failure) at mean age of 25.25±3.4 years. None of them however, had hypogonadotrophism.

Biochemical infertility, though accidentally discovered is a common finding in our environment even among the non-suspecting third party clients in assisted reproduction. Hence, routine pre-marital biochemical fertility profile assessment should be encouraged to diagnose biochemical infertility early before it is too late.

Keywords: Biochemical infertility, Prospective Oocytes' Donors, Assisted Reproductive Unit,

Introduction

The World Health Organization (WHO) defines infertility as "a disease of the reproductive system characterized by the failure to achieve a clinical pregnancy after 12 months or more of regular unprotected sexual intercourse (and there is no other reason, such as breastfeeding or postpartum amenorrhoea).[1] Infertility is considered as primary when the couple has never born a child and secondary when the female partner is unable to conceive during a 12-month period of trial after having born at least one child in the past.

Worldwide, 13 to 15% of couples are infertile.2 Infertility causes worrying, suffering and stigma for the couples who experience this problem. Mostly it is often a big challenge to manage for health professionals. In many communities, the burden of infertility relies on the woman. The subsequent stigma can lead to depression, divorce, ostracism or economical vulnerability.3,4For many patients and couples, not being able to conceive is a challenging obstacle. There are a number of new medical techniques to promote fertility that require medical intervention at various stages of reproduction.5These interventional steps are called assisted reproductive technologies (ART). Assisted reproductive technologies provide a new ability for many couples to overcome infertility and to separate the reproductive process from sexual intercourse.

In most assisted reproductive centers (ours included), we offer "third party reproduction" solutions for those individuals and couples who may benefit from donor assistance. "Third Party Reproduction," according to the American Society for Reproductive Medicine, refers to the use of eggs, sperm or embryos that have been donated by a third person (donor) to enable an infertile individual or couple to become parents. The use of donor eggs, sperm or embryos can

Correspondence to:

Dr. S.A. Biliaminu
Department of Chemical Pathology and Immunology,
University of Ilorin,
Ilorin, Nigeria.
drbiliaminu@gmail.com.
Mobile phone No: - +2348060885920

then be used in ART procedures such as IUI and IVF. "Third Party Reproduction" also includes surrogacy, gestational carrier and traditional surrogacy arrangements.

Historically, the first child born from egg donation was reported in Australia in 1983.6 In July 1983, a clinic in Southern California reported a pregnancy using egg donation, which led to the birth of the first American child born from egg donation on February 3, 1984.7 This procedure was performed at the Harbor UCLA Medical Center and the University of California at Los Angeles School of Medicine.8 In the procedure, which is no longer used today, a fertilized egg that was just beginning to develop was transferred from one woman in whom it had been conceived by artificial insemination to another woman who gave birth to the infant 38 weeks later. The sperm used in the artificial insemination came from the husband of the woman who bore the baby.9

Prior to this, thousands of infertile women, single men and gay male couples had adoption as the only path to parenthood. Advances in IVF and egg donation set the stage to allow open and candid discussion of oocyte and embryo donation as a common practice.8,9 This breakthrough has given way to the donation of human oocytes and embryos as a common practice similar to other donations such as blood and major organ donations.

About 15% of all IVF procedures are done with donated eggs. Whether the female partner no longer has viable eggs, has premature ovarian failure or has had a number of failed IVF attempts with her own eggs, donor eggs may be the right choice to building a family. In general, any woman with a medical or genetic indication for using an egg donor can be a recipient, if there are no medical contraindications to pregnancy.

The procedures for the donor and the medications given to her are identical to the procedures and medications used in autologous IVF (i.e., IVF on patients who are using their own eggs). The egg donor thus has the same low risk of complications from IVF as an autologous IVF patient would, such as bleeding from the oocyte recovery procedure and reaction to the hormones used to induce hyper-ovulation (producing more than one egg), including ovarian hyper-stimulation syndrome (OHSS) and, rarely, liver failure.10

Donor selection is usually diverse and all prospective egg donors should be thoroughly screened and educated on the process of egg donation. The guidelines set forth by the American Society of Reproductive Medicine (ASRM) and the Society for Assisted Reproductive Technology (SART) as well as FDA regulations for egg donation and egg donor compensation are strictly advised to be followed. It is also advised that women who truly want to help others have a child and have passed appropriate physical, genetic and psychological screening should be selected as oocytes' donors.

Prospective oocytes' donors are biochemically screened apart from genetic, physical and psychosocial screening to ensure their suitability. In as much as the "Third Party Reproduction", subjects that is the oocytes' donors are also human beings they may not be exonerated from biochemical infertility. Hence, the aim of this study was therefore to evaluate prevalence and pattern of biochemical abnormalities in prospective oocytes' donors at our Assisted Fertility Center.

Materials and Methods

The study was a retrospective, cross sectional one done at the Assisted Reproductive Unit of the University of Ilorin Teaching Hospital, Ilorin. A total number of forty-eight prospective oocytes' donors who presented between June 2012 and December 2016 at the University of Ilorin Teaching Hospital Assisted Reproductive Unit, Nigeria for possible recruitment as third party subjects for assisted reproductionprocedures had their fasting blood samples collected for fertility profile assay. Serum fertility profile were analyzed using Accubind ELISA Kits manufactured by Monobind Inc. Lake Forest, United States of America. The kits were supplied by NUMS Diagnostics Nigeria Ltd. Suleja, Niger State; Nigeria. This was done as part of their routine laboratory tests to ascertain their suitability for the procedures. Other descriptive parameters were extracted from their records at the center.

Statistical Analysis

Statistical data relating to age of the prospective oocytes' donors, serum fertility profile levels as well as the biochemical infertility classification were extracted from their records at the center. Data analysis was done using SPSS version 20.

Results

A cross-sectional study of forty-eight prospective oocytes' donors who presented between June 2012 and December 2016 at the University of Ilorin Teaching Hospital Assisted Reproductive Unit, Nigeria for possible recruitment as third party subjects for assisted reproduction procedures had their fasting blood samples collected for fertility profile assay.

The mean age for all the 48 prospective oocytes' donors in this study was 22.63±2.28 years, the youngest of them being 19 while the oldest was 30 years old. The mean±SD of all the components of the fertility profile that is the serum FSH, LH, Prolactin, Progesterone, Estradiol and Testosterone were as shown in Table 1.

Table 2 shows mean±SD ofage and biochemical fertility profile of biochemically normal

prospective oocytes' donors. They were 21(43.17%) in number. All the components of the fertility profile that is the serum FSH, LH, Prolactin, Progesterone, Estradiol and Testosterone were biochemically suggestive of normogonadotrophic normogonadism.

Table 3 shows mean±SD of age and biochemical fertility profile of hyper-prolactinaemic prospective oocytes' donors. They were 9(18.75%) in number. The fertility profile is biochemically suggestive of hyper-prolactinaemia.

Table 4 shows mean±SD of age and biochemical fertility profile of prospective oocytes' donors with PCOS. They were 14(29.17%) in number. The fertility profile is biochemically suggestive of PCOS most especially the FSH, LH, LH:FSH ratio and Testosterone.

Table 5 shows mean±SD ofage and biochemical fertility profile of prospective oocytes' donors with hypergonadotrophism (premature ovarian failure). They were 4(8.33%) in number. All the components of the fertility profile that is the serum most especially FSH, LH, Progesterone, and Estradiol were in keeping with hypergonadotrophism (premature ovarian failure).

Table 1: Age and Biochemical Fertility Profile of all Prospective Oocytes Donors

Parameters	N	Minimum	Maximum	Mean	Std.
Age(Years)	48	19.00	30.00	22.63	2.28
FSH(mIU/ml)	48	.13	47.00	7.42	8.03
LH(mIU/ml)	48	1.30	73.00	10.65	12.26
LH:FSHRatio	48	.40	165.20	6.00	24.19
Prolactin(ng/ml)	48	2.30	337.50	26.51	49.60
Progesterone(ng/ml)	48	.11	600.00	16.27	86.48
Estradiol(ng/ml)	48	.24	3000.00	183.82	451.31
Testosterone(ng/ml)	48	.06	5.70	.88	1.03

Table 2. Age and Biochemical Fertility Profile of Biochemically Normal Prospective Oocytes Donors

Parameters	N	Minimum	Maximum	Mean	Std. Deviation
Age(Years)	21	19.00	28.00	21.95	2.25
FSH(mIU/ml)	21	1.70	12.60	5.30	2.85
LH(mIU/ml)	21	1.30	16.00	5.27	3.10
LH:FSH Ratio	21	.50	1.60	1.06	.29
Prolactin(ng/ml)	21	5.70	18.40	12.07	4.01
Progesterone(ng/ml)	21	.11	37.00	4.02	8.77
Estradiol(ng/ml)	21	19.00	220.00	104.5	65.32
Testosterone(ng/ml)	21	.10	.86	.49	.22

Table 3. Age and Biochemical Fertility Profile of Hyperprolactinaemic Prospective Oocytes' Donors

Parameters	N	Minimum	Maximum	Mean	Std. Deviation
Age(Years)	9	20.00	26.00	22.78	2.17
FSH(mIU/ml)	9	2.00	12.00	6.50	3.32
LH(mIU/ml)	9	2.00	11.00	6.21	2.54
LH:FSH Ratio	9	.60	1.30	1.00	.25
Prolactin(ng/ml)	9	19.70	95.00	40.50	26.36
Progesterone(ng/ml)	9	.11	1.10	.24	.33
Estradiol(pg/ml)	9	10.00	60.00	33.67	15.49
Testosterone(ng/ml)	9	.20	.85	.43	.18

Table 4. Age and Biochemical Fertility Profile of Prospective Oocytes' Donors with PCOS

Parameters	N	Minimum	Maximum	Mean	Std. Deviation
Age(Years)	14	20.00	25.00	22.79	1.63
FSH(mIU/ml)	14	.13	30.00	6.25	7.58
LH(mIU/ml)	14	4.30	73.00	19.10	17.20
LHF:SH Ratio	14	2.00	165.20	18.15	43.49
Prolactin(ng/ml)	14	2.30	337.50	43.18	87.11
Progesterone(ng/ml)	14	.11	60.00	7.76	15.75
Estradiol(pg/ml)	14	.24	3000.00	368.0	789.88
Testosterone(ng/ml)	14	.32	5.70	1.96	1.41

Discussion

Infertility, according to the World Health Organization (WHO) defines it as "a disease of the reproductive system characterized by the failure to achieve a clinical pregnancy after 12 months or more of regular, unprotected sexual intercourse (and there is no other reason, such as breastfeeding or postpartum amenorrhoea).1Infertility causes worrying, suffering and stigma for the couples who experience this problem.Assisted reproductive technologies provide a new ability for many couples to overcome infertility and to separate the reproductive process from sexual intercourse.

Advances in IVF and egg donation set the stage to allow open and candid discussion of oocytes and embryos donation as a common practice.8, 9 This breakthrough has given way to the donation of human oocytes and embryos as a common practice similar to other donations such as blood and major organs donations. About 15% of all IVF procedures are done with donated eggs. Whether the female partner no

longer has viable eggs, has premature ovarian failure or has had a number of failed IVF attempts with her own eggs, donor eggs may be the right choice to building a family. In general, any woman with a medical or genetic indication for using an egg donor can be a recipient, if there are no medical contraindications to pregnancy.

Usually, prospective oocytes' donors are biochemically screened apart from genetic, physical and psychosocial screening to ensure their suitability. In as much as the "Third Party Reproduction", subjects that is the oocytes' donors are also human beings they may not be exonerated from biochemical infertility. Hence, the aim of this study was therefore to evaluate prevalence and pattern of biochemical abnormalities in prospective oocytes' donors at our Assisted Fertility Center.

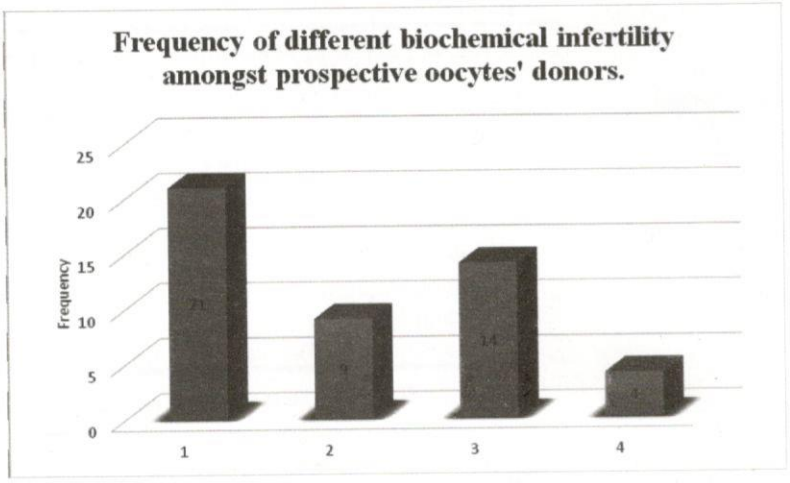
In this study, which happens to be a retrospective cross-sectional one, a total number of forty-eight prospective oocytes' donors who presented between June 2012 and December 2016 at the University of Ilorin Teaching Hospital Assisted Reproductive Unit, Nigeria for possible recruitment as third party subjects for assisted reproduction procedures had their fasting blood samples collected for fertility profile assay. The mean age for all the 48 prospective oocytes' donors in this study was 22.63±2.28 years, the youngest of them being 19 while the oldest was 30 years old.

The success of oocyte donation may be influenced by various factors, including the donor's age, quality and number of embryos transferred, and recipient's age and endometrial receptivity; donor age is undoubtedly the most important factor contributing to treatment success.11The mean donor age in this study was lower than that of Matthew et al which was 29.6 ± 5.1 years (range 20-41).12 The youngest in their study which was 19 years was almost equal to 18 years in our study.However, the lowest age of 18 years in our center is still shows compliance with American Society for Reproductive Medicine's minimum age threshold of 18 years for oocytes donors.13

Table 5. Age and Biochemical Fertility Profile of Hypergonadotrophic Prospective Oocytes' Donors

Parameters	N	Minimum	Maximum	Mean	Std. Deviation
Age(Years)	4	22.00	30.00	25.25	3.40
FSH(mIU/ml)	4	14.00	47.00	24.75	15.37
LH(mIU/ml)	4	10.00	45.00	20.25	16.74
LH:FSH Ratio	4	.40	1.10	.79	.31
Prolactin(ng/ml)	4	4.00	23.80	12.53	9.73
Progesterone(ng/ml)	4	.11	2.60	.73	1.25
Estradiol(pg/ml)	4	.28	220.00	79.57	96.40
Testosterone(ng/ml)	4	.06	.45	.28	.16

Chart 1.



1= Biochemically normal prospective oocytes' donors,2= Hyperprolactinaemic prospective oocytes' donors, 3=Prospective oocytes' donors with PCOS, 4=Hypergonadotrophic prospective oocytes' donors

From this study, biochemical fertility profile of 21(43.17%) of prospective oocytes' donors were within reference limits thus suggesting normogonadotrophic normogonadism. By virtue of having this biochemical status, it does qualified them as suitable oocytes' donors having scaled through in other preliminary screening investigations.

In this study, the fertility profile was biochemically suggestive of hyper-prolactinaemia in 9(18.75%) of our subjects. Eight out of these hyper-prolactinaemic were having PCOS. Elevated serum prolactin is a common finding in PCOS patients. The remaining one hyper-prolactinaemic subject was actually naïve of 10 weeks' cyesis. This figure was higher than the prevalence of hyper-prolactinaemia in the study done in infertile women at University of Ilorin Teaching Hospital (UITH), Ilorin.14 It was also lower than similar study done in pre-menopausal female donors.15The higher prevalence gotten in this study might be connected with the large number of PCOS found in this study with concomitant PCOS.

A total number of 14(29.17%) prospective oocytes' donors were biochemically diagnostic of PCOS most especially the LH:FSH ratio and Testosterone in this study. This prevalence was

significantly higher than in the study among privately insured in USA 2003 and 2008.16This might not be unconnected with the fact that the mean age of subjects in this study were in the median age of PCOS.16

Biochemical fertility profile of prospective oocytes' donors in this study was suggestive of hypergonadotrophic hypogonadism (premature ovarian failure) in 4(8.33%). This figure was lower than the prevalence of hypergonadotrophic hypogonadism (premature ovarian failure) in the study done in infertile women at University of Ilorin Teaching Hospital (UITH), Ilorin.14The lower prevalence gotten in this study might not be unconnected with the fact that the mean age of the subjects was lower than that of the infertile women studied at UITH.

Conclusion

From this study we concluded that biochemical infertility is not only a common finding in our environment in married infertile or subfertile women, it is also a common finding even among the non-suspecting third party clients in assisted reproduction. Hence, routine pre-marital biochemical fertility profile assessment should be encouraged to diagnose biochemical infertility early before it is too late.

References

1. Cooper T.G, Noonan E, von Eckardstein, et al. World Health Organization reference values for human semen characteristics. Hum Reprod Update. 2010;16:231–245.
2. World Health Organozation. Report of the Meeting on the Prevention of Infertility at the Primary Health Care Level. WHO, Geneva; 1983. WHO/MCH/1984.4
3. Sciarra J. Infertility: an international health problem. Int J Gynaecol Obstet 1994; 46(2): 155-63.
4. Nana P.N, Wandji J.C, Fomulu J.N, Mbu R.E, Leke R.J, Woubinwou J. Aspects psycho-sociaux chez patients infertiles à la maternite principale de l'hopital Central de Yaoundé, Cameroun. Clinics in Mother and Child Health 2011; 8: 1-5.
5. John M. Shane, Evaluation and Treatment of Infertility, 45 CLINICALSYMP. (1993); MERK MANUAL 16th Edition; 1992; 1772-73.
6. Wendy K. A Brief History of Donor Conception. 2016.
7. Blakeslee S. "Infertile Woman Has Baby Through Embryo Transfer". (1984-02-04). The New York Times.
8. Friedrich O, Constable A. Samghabadi R. (1984-09-10). "Medicine: A Legal, Moral, Social Nightmare"Time.
9. Wallis C. (1984-09-10). "The New Origins of Life". Time.
10. Mark V.S, Matthew A.A. Egg and embryo donation. In: David K.G, Ariel W, Colin M.H, Zeev S. eds.Textbook of Assisted Reproductive Techniques, Laboratory and Clinical Perspectives. London: Informa. 2010: 807-816.
11. Faddy M, Gosden R, Ahuja K, Elder K. Egg sharing for assisted conception: a window on oocyte quality. Reproductive BioMedicine. (2011). 22 (1) 88–93.
12. Matthew A.C, Steven R.L, Mark V.S. Donor age is paramount to success in oocyte donation. Hum Reprod (1999) 14 (11): 2755-2758.
13. Hillary B.A, Roberta M.B, Aaron D.L. Compliance with donor age recommendation in oocyte donor recruitment advertisements in the USA. Reproductive BioMedicine (2013) 26: 400–405.
14. Akande A.A, Idowu A.A, Jimoh A.K. Biochemical infertility among females attending University of Ilorin Teaching Hospital, Nigeria. (2009);12(1):20-24.
15. , Sanchón R, Martínez-García MÁ, Martínez-Bermejo E, Escobar-Morreale HF. Prevalence of hyperprolactinaemia in female premenopausal blood donors. Clin Endocrinol (Oxf). (2013) 79: (4):545-9.
16. Ekwutosi M.O, Hooper W.C, Hani K.A. Hussain R.Y,Sheree L.B. Prevalence of polycystic ovary syndrome among the privately insured, United States, 2003-2008. American Journal of Obstetrics and Gynecology. 207(4) 2012. 299.