RISING REPRODUCTIVITY IN ADVANCED AGE: THE INTERNIST'S INVOLVEMENT

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ABSTRACT

Background: *As the world ages, so is there advancement in knowledge, science and have improved the quality of life of individuals, thus leading to an increase in life expectancy in almost all the regions of the world. Reproduction in elderly females is on the rise due to the acceptability of assisted reproductive technology in treatment of infertility. This is likely to result in an increase in interventions by the internist in this age group during pregnancy.*

Aim: *To review the involvement of the internist in the management of advanced age pregnancy and its outcome.*

Methods and Materials: *Journals, newspaper and magazine publications of case reports of women who were 60 years and above who gave birth to live babies worldwide were analyzed. An internet-based search of credible websites was also done to verify information and analysis of various factors were done. It is a retrospective cross- sectional study of women aged 60 years and above who had live births worldwide.*

Results: *There were 60 persons aged 60 years and above gathered from the publications, 96.7% of these patients had assisted reproduction. The commonest age range was 60-64 years. Primary infertility without children in couples was the cause of seeking in vitro fertilization in 50% of cases. 10% of the pregnancies were associated with medical complications such as diabetes and hypertension in 57.7% of documented cases, birth weights were low.*

Conclusion: *The management of pregnancy of advanced maternal age is multi disciplinary of which the internist plays an important role.*

Key words: *Advanced age, Fertility, Internist, Reproduction.*

INTRODUCTION

Reproduction in the elderly females is on the increase worldwide, despite surpassing menopause, a time which majority of women aged 60 years and above no longer produces eggs. This changing trend is due to the availability, accessibility, affordability and acceptability of in vitro fertilization(IVF) as a means of curbing infertility amongst different ethnicities and people of different religious beliefs.

Infertility which is defined demographically by the World Health Organization as the

inability to achieve pregnancy with a live baby after half a decade of consistent copulation without contraceptives usage with continuous sustenance of the desire to procreate [1] in couples depends on both male factors and female factors in terms of their reproductive organs. Clinically it is defined as twelve calendar months of no viable live birth after regular sustained sexual intercourse between a couple. The term fecundity is more specific to live births while infertility is regarded to pregnancy rates but both can be used interchangeably.[1]Primary infertility is considered as the inability to produce a live birth despite previous miscarriages or still birth.[1] The age of both the man and woman has also been shown to be a contributory factor to the ability to conceive thus the older one becomes the greater the decline in fertility. It is also a known fact that there are chronic medical illnesses such as diabetes; obesity and tuberculosis that may also affect the ability of couples to conceive.[2,3,4]Lifestyles such as chronic smoking and chronic alcohol consumption have been shown to affect fertility.[5,6,7]

Internal Medicine is the specialty that deals with management of chronic medical diseases comprising of several subspecialties and the physician in this field is called the internist. The internist is usually called when there is a medical complication in pregnancy but with the increasing cases of achieving pregnancy at an advanced age of sixty years and above particularly in elderly females the internist is likely going to be more involved in co-managing these patients with the obstetricians prior to pregnancy complications.

The Internal medicine physician or the internist's involvement in management of advanced age pregnancy can be divided into three segments; the preconception, intra conception (during pregnancy) and post conception/post- delivery periods. The internist, depending on the specialty will be seeing more elderly patients in the future to come, receiving referrals from the family physicians or general practice doctors. The internist is well grounded in matters of medical ailments that cause infertility, the kind of treatment needed by the elderly mothers and complications of the medical interventions offered.[8] The internist would also be involved in preconception counseling and in interventions for preventable ailments that cause infertility. Almost one fifth of pregnant women are said to have one medical illness which may be fatal to both the mother and fetus this is the basis for the battery of tests prior to assisted reproductive intervention.[8]The Internist requested for may be the general internal medicine physician or a specialist in a particular field who will work closely with the maternal-fetal-medicine specialist who is usually a qualified obstetrician and gynecologist.[9]

Therefore, this study aimed review the involvement of the internist in the management of advanced age pregnancy and its outcome.

METHODS AND MATERIALS

The study is a retrospective cross-sectional study of elderly women with live births. Journals, newspaper and magazine publications of case reports of women who were 60 years and above who gave birth to

live babies worldwide were analyzed. An internet-based search of credible websites such as www.guardian.ng, www.dailymail.co.uk, www.medicaldaily.com,www.bbc.news.com, www.punchng.com, www.pulse.ng, www.guinessworldrecords.com, www.pubmed.gov,www.cnn.com, www.thesun.co.ukand www.cbs.com was also done to verify information and analysis of various factors were carried out. These factors were the age of the woman, means of conception, reason for IVF at the time, birth weight of the baby, gestational age at delivery, pregnancy outcome and medical complications noticed during the pregnancy or puerperal period.

RESULTS

Table1: Reason for IVF

Reason	Frequency	%
Primary infertility without children from either partner	29	50.0
Primary infertility with children from previous union by one or both partners	16	27.6
Secondary infertility with loss of previous children(two were refused adoption)	3	5.2
Secondary Infertility without loss of children(two were for sex selection)	5	8.6
Gestational Surrogacy	5	8.6
Total	58	100

Primary Infertility was the major cause of infertility as observed in half of the cases.

Table 2: Causes of Primary Infertility / sterility without children

Factors	frequency	%
Male factors(chronic smoking, infrequent copulation due to job)	1	3.5
Female factors(tuberculosis caused sterility)	1	3.5
Placenta praevia(recurrent)	1	3.5
Spontaneous abortions	1	3.5
Not Stated	25	86
Total	29	100

Male and female causes were both contributory to infertility.

Table3: Medical complications

Medical complications	Frequency	%
Pregnancy Induced hypertension(PIH)	2	33.3
Gestational Diabetes(GDM)	1	16.7
GDM+PIH	1	16.7
Renal Insufficiency	1	16.7
Stomach cancer	1	16.7
Total	6	100

Diabetes and hypertension were major medical complications seen.

Table 4: Pregnancy outcomes (documented cases)

Gestational age	Freq.	%	Birth weight (BW)	Freq.	%	Pregnancy outcomes	Freq	%	Sex	Freq	%
Preterm	7	63.7	Low BW	15	57.7	singleton	47	78.3	male	30	58.8
Normal	4	36.3	Normal BW	11	42.3	multiple	13	21.7	female	21	41.2
Post term	0	0	Macrosomia	0	0	-	-	-	-	-	-
Total	11	100		26	100		60	100		51	100

Preterm, low birth weight, and male babies were more in number comparatively.

Table 5: Gestation (number of fetus)

Type	Frequency	%
Singleton	47	78.3
Twins	9	15.0
Triplets	3	5.0
Quadruplets	1	1.7
Total	60	100

Singleton babies were predominant in pregnancy outcomes.

The modal age group was 60-64 with 73.3% (44) of women falling within this group, followed by 65-69 with 21.7%(13) and those above 70 with 5%(3).Half of these women with their partners have not conceived a child before in their live time. About 8.6% of these women were gestational surrogates for their close relatives. The period of primary infertility ranged from 20-60 years in those who had been living with their partners. The primary infertility periods of 30-39years and 40-59 years had the highest number of women of 4 each out of the 11 documented cases. A greater percentage of the women-72.4% (42) used sperm from their partners while 15.5% (9) had anonymous sperm donors and 12.1% (7) had close relatives acting as sperm donors. Majority of women 96.7% (58) had Caesarean section as their mode of delivery.

DISCUSSION

The modal age range of women with live births aged 60 years and above was 60-64. This is a reflection of the persistent desire for women to be mothers despite being above the universal accepted reproductive age group for childbearing which is regarded as 15-44 years. The internist might not be directly involved in ethical issues involving the decision to perform an IVF for an elderly female patient but must be aware of them and also be aware of other ethical guide lines concerning care and treatment as a whole for the patient.

Most of the women had IVF. Prior to IVF, the women are treated with hormones which help in preparation of the endometrium for the growth and sustenance of the pregnancy. The internists(specifically the endocrinologists) are involved in treating hormonal imbalance in women with post-menopausal symptoms. Therefore, the internist's expertise may be sought during the process of IVF.

Primary infertility was the main reason for seeking for children despite old age in majority of the women(seeTable1). The causes of infertility may be multi-factorial in couples. It could be inherited or acquired medical problems or due to bad lifestyle habits such as smoking and excessive

alcoholic intake as it was in the case of one male partner (see Table 2). Endocrine causes of infertility include Addison's disease, Asherman's syndrome, thyroid problems either hyper or hypo, hypopituitarism, premature ovarian disease and polycystic ovarian disease which can all cause prolong infertility in couples. Obesity is a challenge in most patients which can be a clinical feature of the cause of infertility as well as a complication from hormonal therapy during fertility treatment.[2]

Prior to conception, the internist might also be faced with treating co-morbidities as seen in this study, one of the women had sterility resulting from tuberculosis. In such cases the pulmonologist and the infectionologist may be invited to review the patients prior and during pregnancy for resurgence of the disease since pregnancy is an immune-compromised state. The infectionologist in partnership with the community physician and medical microbiologist has to deal with preventing infertility from sexual transmitted infection including HIV. The rheumatologist might also have to evaluate patients for those with recurrent spontaneous abortions particularly if it is occurring in the first trimester of pregnancy which the cause might be due to antiphospholipid syndrome which may reoccur in predisposed elderly females even with donated eggs. The pharmacokinetics and pharmacodynamics of the drugs used in infertility may have to be assessed by the clinical pharmacologist.

The result above states the prolonged periods in which those with primary infertility had waited before being successful at having a life baby. Some may have been on different drugs to boost fertility within this period including herbal medication which may not be very effective and the safety profile is not certain.[10]

More than a quarter of the patients received sperm donation from those who were not their regular sex partners, this goes to show that the quality of sperm is important in achieving pregnancy,[5,7,11,12] although some of them were gestational surrogates to close relatives. Fertilization of the egg is done outside the body with the sperm undergoing different processes to reduce the chances of rejection. Males are known to have viable sperms up to old age but then the quality of sperm declines with age. The reproductive endocrinologist may also sub- specialize in testicular immunology thus would be handling issues such as allergic reactions and antibodies development to sperm; though these are rare ailments, they do occur and can be a cause of infertility.

Major medical complications seen in this study which were hypertension and gestational diabetes (see Table 3).Diabetes and hypertension are two common disorders seen in elderly persons. This finding is similar to the one done amongst women aged 55-63.[13,14] They can also coexist in the same patient(see Table 3). Hypertension is a common complication seen even in pregnancy particularly in older maternal age greater than 35 even without previous chronic medical illness.[15,18]

Pre-eclampsia and eclampsia can also occur

like in any other age group and would be managed by both the internal medicine physician and the obstetrician. They are also known to be on the increase with higher maternal age.[16]In evaluation of the patient prior to in vitro fertilization, the patient is subjected to various cardiac tests such as stress electrocardiography, echocardiography, lipid profile and uric acid levels etc. to assess their cardiovascular fitness in carrying the physical burden of pregnancy. These patients may be referred to the cardiologist for evaluation and treatment of cardiac related health challenges such as hypertension and atherosclerosis. The patient may also need to see other specialists based on the results of screening tests which may warrant medical advice from them on whether the individual is fit to be a candidate for IVF.

Renal insufficiency manifesting as acute kidney injury can complicate any pregnancy even for gestational surrogates as seen in this study. There may be a likely increase in renal insufficiency such as acute renal failure in advanced maternal age due to other increased risk of hypertensive related disorders like preeclampsia and eclampsia.[17] The nephrologists may make their input in management but it usually resolves with adequate rehydration, treatment of infections and assurance. Development of cancers associated with hormonal stimulation in IVF has controversial results with very few studies carried out. The findings mostly suggest ovarian and colonic cancers. These may metastasize to other areas of the body. The oncologist or gastroenterologist or both will co-manage the patient. It is important to note that the risk of ovarian cancers may be increased in nulliparous women.

Almost all the women in this study 96.7% had Caesarean section and this is a very common finding due to both maternal and fetal complications associated with advanced maternal age.[9, 13]They may also have associated medical conditions that may make induction of labour risky; and complications developing postpartum usually require the support of the internist.

Pregnancy in advanced age has been associated with increase in preterm and low birth weight babies. Majority of IVF interventions may result in increase in cesarean deliveries and multiple gestations however singleton pregnancies were seen more in this study(see Tables 4 and 5). This finding is not different from women in other age groups who had IVF.[13] Preterm babies and multiple gestation all are predisposing factors to low birth weight. Low birth weight has been known to be a contributory factor to chronic medical illness later in life such as hypertension, diabetes, renal disease and respiratory illness as well as poor cognitive development.[19] This is a potential area for future research, comparing the development of chronic medical ailments in low birth weight babies and those with normal birth weight born to women aged 60 years and above.

The geriatrician either as an internist or a family medicine physician has the role of seeing the elderly patient as a whole, would also be consulted if geriatric services are

available in such centers. This may be another area of sub-specialty in the field of geriatrics or obstetrics such as having a geriatric obstetrician or an obstetric geriatrician.

LIMITATION

The limitation of this study was that most the data were gotten from online magazines and newspapers and very few journals. There was variation in data concerning some factors such as the age of the women. There was incomplete data for some of the factors assessed for some of the women such as gestational age, pregnancy outcomes, and medical complications. There was paucity of data on other factors such as chronic medical conditions, family history of chronic medical diseases, level of education and causes of infertility which would have added value to the study. The tests of significance could not be done since this is purely a cross-sectional descriptive study done on a group of women who characteristics cannot fairly be compared in the sub age groups due to incomplete data.

CONCLUSION

From preconception to the postpartum period, the internists are important in the management of pregnancy in women of advanced age. The internist also has a futuristic role to play in watching out and strategizing preventive interventions for chronic medical illness in low birth weight babies born to these women.

RECOMMENDATIONS

The increasing fertility rates amongst women in advanced age should cause clinicians whether as physicians or obstetricians to begin to prepare themselves for further research in combating challenges associated with pregnancy in this age group. Guidelines concerning care in this set of pregnant women should be developed by the World Health Organization that will be uniformly implemented in all countries by health care workers.

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