

Awareness and acceptability of invitro fertilization with donor gamete as reproduction alternative for reducing the risk for giving birth to children with sickle cell disease among at risk couples

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Abstract

Background: Sickle cell disease (SCD) is an autosomal recessive genetic disorder of red blood cell which is transferable from parent carriers to their offspring. It is associated with lots of morbidity and mortality. Invitro fertilization (IVF) with donor gamete is an alternative reproduction option for reducing the risk for giving birth to children with SCD. The awareness and acceptability of this option have not been assessed in our environment.

Objective: To assess the awareness and acceptability of IVF with donor gamete as reproduction alternative for reducing the risk for giving birth to children with SCD among at risk couples.

Materials and Methods: Seventy-three biological parents of children with SCD were interviewed with semi-structured questionnaire following consent at the Paediatric Haematology outpatient clinic of ESUT Teaching hospital Parklane, Enugu. Convenient sampling method was used. Data obtained was entered into SPSS version 26 and later exported to SPSS version 29 with which it was analyzed.

Results: Awareness and acceptability (following education) of IVF with donor gamete as reproduction alternative for reducing the risk for giving birth to children with SCD among the respondents were 3 (4.1%) and 25 (34.2%) respectively. Desire for biological children was the commonest reason for acceptance 22 (30.1%) and non-acceptance 40 (54.8%) of the option.

Conclusion: Awareness and acceptability of IVF with donor gamete as reproduction alternative for reducing the risk for giving birth to children with SCD were poor. To improve on both, there is much need for awareness creation and reorientation.

Keywords: Sickle cell disease; Prevention; *In vitro* fertilization; Donor gamete; Awareness; Acceptability

1. Introduction

Sickle cell disease (SCD) is an autosomal recessive genetic disorder of red blood cell which is transferable from parent carriers to their offspring [1]. It is the most common inherited disease worldwide and is associated with anaemia and intermittent severe pain [2]. Globally, it is estimated that about 305,000 babies are born annually with SCD [3]. Report suggests that currently Nigeria has the highest burden of the SCD globally accounting for up to 50% of the new cases in the world [3]. It is estimated that about 50 million people are living with sickle cell disease globally with about 4-6 million of them in Nigeria [1]. One in every four Nigerian has been reported to have the sickle cell trait [4].

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SCD contributes significantly to morbidity and mortality of both paediatric and adult population [1]. For example, it has been reported that about 50%-90% of children born with SCD in low- and middle-income countries of sub-Saharan Africa die before their fifth birthday [4]. These early deaths have been attributed to late diagnosis and delayed prophylactic interventions [3]. About 20% of neonatal mortality and 5% of under-five mortality in the African continent has been reported to result from SCD [5,6]. Also, SCD has been reported to contribute to several obstetric complications and high maternal mortality rates among women of child-bearing age living with SCD in Sub-Saharan Africa [7,8].

The management of SCD in Africa is associated with numerous challenges, including but not limited to insufficient healthcare infrastructure, inadequate access to essential medications like hydroxyurea, and shortage of specialized healthcare providers [9]. One very important aspect of management of complications of SCD is blood transfusions which is however often hampered by inadequate supply of blood for transfusion and the risk of transfusion-transmissible infections [10]. Also, the drug hydroxyurea has shown demonstrable efficacy in reducing severity of SCD but its poor availability and affordability remain significant barriers [11]. Bone marrow transplantation can potentially provide cure for SCD but are largely inaccessible due to high costs and procedural complexities [9].

In the light of the foregoing, any intervention capable of reducing the introduction of new cases of SCD into the population especially among parents of affected children is expected to be very much welcome. Interestingly, since SCD is a disease transmitted only when there is fertilization between the gametes of couples who carry the sickle cell trait, conception through invitro fertilization (IVF) with donor gamete from an individual without the sickle cell trait removes the possibility of giving birth to a child with SCD. For example, such couple may decide to use the sperm from the male partner and an egg from a female donor who do not have sickle cell trait. Globally, there is scarcity of study on awareness and acceptability of invitro fertilization with donor gamete as a method for reducing the risk for giving birth to children with sickle cell disease among parents of children with sickle cell disease. Schultz and colleagues [12] in America reported that awareness of IVF with donor gamete as reproduction alternative for reducing the risk for giving birth to children with sickle cell disease among at risk parents was very much limited and that only 2 out of 18 parents of children with sickle cell disease interviewed accepted invitro fertilization with donor gamete as reproduction alternative for reducing the risk for giving birth to children with SCD. Despite the potential of invitro fertilization with donor gamete to reduce the number of newborns with SCD, awareness and acceptability of the option among parents of children with SCD remains largely unassessed. It is against this background that this study was set out to assess the awareness and acceptability of invitro fertilization with donor gamete as reproduction alternative for reducing the risk for giving birth to children with SCD among parents of children with sickle cell disease accessing care at the Paediatric Haematology outpatient clinic of Enugu State University of Science and Technology (ESUT) Teaching Hospital Parklane Enugu, Enugu State Nigeria.

2. Materials and Methods

This study was part of a bigger study on the alternative reproduction options for reducing the risk for giving birth to children with sickle cell disease among parents of children with sickle cell disease that accessed care at Paediatric Haematology outpatient clinic of ESUT Teaching hospital Parklane Enugu during the study period. It was a hospital based cross sectional study and spanned from September, 2022 to July, 2024. ESUT Teaching hospital is located in the center of Enugu Metropolis. It serves as a referral center for most states in the South East Nigeria. The department of Paediatrics is one of the four major departments of the hospital and Paediatric Haematology clinic is one of the outpatient clinics in the department of Paediatrics. The Paediatric haematology clinic takes care of patients up to 18years of age and runs from 8:00 am in the morning to 4:00pm in the evening every Monday. The clinic is managed by a consultant Paediatric haematologist, resident doctors, nurses and other allied health workers. Haematology outpatient clinic is a fairly busy clinic however they also attend to other paediatric cases other than haematology cases.

The target population was biological parents of children with sickle cell disease who received care at the Paediatric haematology outpatient clinic over the study period hence only biological parents of sickle cell children were included in the study. Written informed consent was obtained from all the respondents and they were reassured of the confidentiality of information provided. For each of the respondents the interview was conducted in two parts with well-structured interviewer administered questionnaire. In the first part, the respondents were interviewed with the beginning part of the questionnaire which contained questions on their sociodemographic and other respondents' characteristics as well as their awareness of invitro fertilization with donor gamete as a reproduction alternative for reducing the risk for giving birth to children with SCD. After the initial part of the interview each of the respondents was given adequate counselling and education on IVF with donor gamete as a means to help couples with SCD trait to reduce the risk for giving birth to children with sickle cell disease. Subsequently, the remaining part of the questionnaire to assess for the acceptability of IVF with donor gamete as a reproduction alternative for reducing the risk for giving birth

to children with SCD were administered. Ethical clearance for the study was obtained from the ethics committee of ESUT Teaching hospital Parklane, Enugu. The questionnaire was pretested and all ambiguity removed.

Data collected were entered into SPSS version 26 and later exported to SPSS version 29 with which it was analyzed. Data cleaning was performed to ensure completeness and accuracy prior analysis. Categorical variables, including awareness and acceptability of invitro fertilization with donor gamete were summarized using frequencies and percentages.

Associations between categorical variables were examined using Fisher's exact test with statistical significance set at $p < 0.05$.

3. Results

Seventy-three respondents were interviewed. Of these 65(89%) were females, while 8(11%) were males. Majority were 35 years and above 51(69.9%), urban dwellers 62(84.9%) and of the Igbo tribe 72(98.6%). All the respondents were Christians and majority were Catholics 45(61.6%). The rest of the respondents' characteristics are as outlined in Table 1 below.

Table 1 Socio-demographic characteristics of the respondents

Respondents' Characteristics	Variables	Frequency (n = 73)	Percentage (%)
Age	< 35 years	22	30.1
	≥ 35 years	51	69.9
Sex	Male	8	11
	Female	65	89
Residence	Rural	11	15.1
	Urban	62	84.9
Tribe	Igbo	72	98.6
	Others	1	1.4
Christian Denominations	Catholics	45	61.6
	Anglicans	8	11
	Pentecostals	18	24.7
	Others	2	2.7
Educational Status	≤ Primary	6	8.2
	Secondary	36	49.3
	≥ Tertiary	31	42.5
Employment Status	Unemployed	7	9.6
	Employed	66	90.4
Marital Status	Married	64	87.7
	Never Married	1	1.4
	Separated/Widow/Widower	8	11.0
Duration of Marriage	< 15 years	45	61.6
	≥ 15 years	27	37
	Not applicable	1	1.4
Number of Children	Yes	24	32.9
	No	49	67.1

Table 2 Impact of SCD on respondents' families

Respondent Characteristics	Variable	Frequency (n=73)	Percentage (%)
Number of children with SCD	1	60	82.2
	2	12	16.4
	3	1	1.4
Child died of SCD	Yes	17	23.3
	No	56	76.7

Majority of the respondents 60 (82.2%) had one child with SCD while up to 17 respondents (23.3%) had lost at least a child to SCD.

Table 3 Awareness and acceptability of IVF with donor gamete as reproduction alternative for reducing the risk for giving birth to children with SCD among the respondents

	Yes (n = 73)	Percentage	No (n = 73)	Percentage
Awareness of IVF with donor gamete as reproduction alternative	3	4.1	70	95.9
Acceptability of IVF with donor gamete as reproduction alternative	25	34.2	48	65.8

As shown on Table 3 above only 3 respondents (4.1%) were aware of IVF with donor gamete as reproduction alternative for reducing the risk for giving birth to children with SCD while the option was acceptable to only 25 respondents (34.2%).

Table 4 shows that of all the respondent characteristics, only marital status and duration of marriage were significantly associated with awareness of IVF with donor gamete as reproduction alternative for reducing the risk for giving birth to children with SCD.

Also, Table 5 shows that Christian denomination of the respondents was the only respondent characteristic that was significantly associated with acceptability of IVF with donor gamete as reproduction alternative for reducing the risk for giving birth to children with SCD

Table 4 Relationship between awareness of IVF with donor gamete as reproduction alternative for reducing the risk for giving birth to children with SCD and respondents' characteristics

Respondents' Characteristics	Variables	Aware of IVF with Donor gamete		Unaware of IVF with donor gamete		p-value
		Frequency	Percentage	Frequency	Percentage	
Age	< 35 years	2	2.7	20	27.4	0.214
	≥ 35 years	1	1.4	50	68.5	
Sex	Male	0	0	8	11	1.000
	Female	3	4.1	62	84.9	
Residence	Rural	0	0	11	15.1	1.000
	Urban	3	4.1	59	80.8	
Tribe	Igbo	3	4.1	69	94.5	1.000

	Others	0	0	1	1.4	
Christian Denominations	Catholics	2	2.7	43	58.9	0.485
	Anglicans	1	1.4	7	9.6	
	Pentecostals	0	0	18	24.7	
	Others	0	0	2	2.7	
Educational Status	≤ Primary	0	0	6	8.2	0.686
	Secondary	1	1.4	35	47.9	
	≥ Tertiary	2	2.7	29	39.7	
Employment Status	Unemployed	1	1.4	6	8.2	0.264
	Employed	2	2.7	64	87.7	
Marital Status	Married	1	1.4	63	86.3	0.010*
	Never Married	1	1.4	0	0	
	Separated/ Widow/ Widower	1	1.4	7	9.6	
Duration of Marriage	< 15 years	2	2.7	43	58.9	0.022*
	≥15 years	0	0	27	37	
	Not applicable	1	1.4	0	0	
Number of Children	≤ 2	2	2.7	22	30.1	0.250
	≥ 3	1	1.4	48	65.8	
Number of Children with SCD	1	2	2.7	58	79.5	0.450
	2	1	1.4	11	15.1	
	3	0	0	1	1.4	
Child died of SCD	Yes	0	0	17	23.3	1.000
	No	3	4.1	53	72.6	

* = Statistically significant

Table 5 Relationship between acceptance of IVF with donor gamete as reproduction alternative for reducing the risk for giving birth to children with SCD and respondents' characteristics

Respondents' Characteristics	Variables	Aware of IVF with Donor gamete		Unaware of IVF with donor gamete		p-value
		Frequency	Percentage	Frequency	Percentage	
Age	< 35 years	6	8.2	16	21.9	0.592
	≥ 35 years	19	26.0	32	43.8	
Sex	Male	3	22	5	6.8	1.000
	Female	22	30.1	43	58.9	
Residence	Rural	4	5.5	7	9.6	1.000
	Urban	21	28.8	41	56.2	

Tribe	Igbo	25	34.2	47	64.4	1.000
	Others	0	0	1	1.4	
Christian Denominations	Catholics	17	23.3	28	38.4	0.016*
	Anglicans	4	5.5	4	5.5	
	Pentecostals	2	2.7	16	21.9	
	Others	2	2.7	0	0	
Educational Status	≤ Primary	3	4.1	3	4.1	0.617
	Secondary	11	15.1	25	34.2	
	≥ Tertiary	11	15.1	20	27.4	
Employment Status	Unemployed	2	2.7	5	6.8	1.000
	Employed	23	31.5	43	58.9	
Marital Status	Married	22	30.2	42	57.5	0.406
	Never Married	1	1.4	0	0	
	Separated/ Widow/ Widower	2	2.7	6	8.2	
Duration of Marriage	< 15 years	15	20.5	30	41.1	0.545
	≥15 years	9	12.3	18	24.7	
	Not applicable	1	1.4	0	0	
Number of Children	≤ 2	9	12.3	15	20.5	0.794
	≥ 3	16	21.9	33	45.2	
Number of Children with SCD	1	19	26.0	41	56.2	0.306
	2	5	6.8	7	9.6	
	3	1	1.4	0	0	
Child died of SCD	Yes	7	9.6	10	13.7	0.564
	No	18	24.7	38	52.1	

* = statistically significant

Table 6 Pattern of reasons for acceptance of IVF with donor gamete as reproduction alternative for reducing the risk for giving birth to children with SCD among the respondents

Reasons	Yes		No		Not Applicable	
	Frequency	Percentage (%)	Frequency	Percentage (%)	Frequency	Percentage (%)
Cultural belief	2	2.7	23	31.5	48	65.8
Societal acceptance	4	5.5	21	28.8	48	65.8
Desire for biological child	22	30.1	3	4.1	48	65.8

Nature of the process	9	12.3	16	21.9	48	65.8
Cost	2	2.7	23	31.5	48	65.8
Religious belief	4	5.5	21	28.8	48	65.8

Table 7 Pattern of reasons for non-acceptance of IVF with donor gamete as reproduction alternative for reducing the risk for giving birth to children with SCD among the respondents

Reason	Yes		No		Not Applicable	
	Frequency	Percentage (%)	Frequency	Percentage (%)	Frequency	Percentage (%)
Cultural belief	4	5.5	44	60.3	25	34.2
Societal acceptance	6	8.2	42	57.5	25	34.2
Desire for biological child	40	54.8	8	11.0	25	34.2
Nature of the process	17	23.3	31	42.5	25	34.2
Cost	3	4.1	45	61.6	25	34.2
Religious belief	4	5.5	44	60.3	25	34.2

Table 6 and Table 7 show that the desire for biological children was the commonest reason for both acceptance and non-acceptance of IVF with donor gamete as reproduction alternative for reducing the risk for giving birth to children with SCD among the respondents.

4. Discussion

The morbidity and mortality rates associated with SCD is so enormous that any effort geared towards reducing the burden of the disease is expected to be a welcome contribution. As such this study was carried out to assess the awareness and acceptability of invitro fertilization with donor gamete as a reproduction alternative for reducing the risk for giving birth to children with SCD among at risk couples.

Majority of the respondents were females, 35 years and older, of Igbo tribe and urban dwellers. The finding of majority of the respondents being urban dwellers is understandable as the study center is located within Enugu Metropolis hence the immediate catchment area is essentially urban. Also, the dominant tribe in Enugu the city of the study center is Igbo hence it came as no surprise that majority of the respondents were of the Igbo tribe. Majority of the respondents being 35 years and above is also understandable since the target population was parents of sickle cell children that accessed care at ESUT Teaching hospital Parklane Enugu during the study period.

All the respondents were Christians with majority belonging to the Catholic denomination. This is in line with the reality on ground as Christianity is the dominant religion in region of the study center [13].

Awareness of IVF with donor gamete as reproduction alternative for reducing the risk for giving birth to children with SCD was very low among the respondents. Only 4.1% of the respondents were aware of IVF with donor gamete as reproduction alternative for reducing the risk for giving birth to children with SCD. This is lower than that reported by Schultz and colleagues in the United State of America who found that 2 out of 18 parents of children with SCD interviewed (11.1%) were aware of IVF with donor gamete as reproduction alternative for reducing the risk for giving birth to children with SCD [12]. Awareness of 4.1% as found in this study is also much less than that reported by Darbari and colleagues (44%) following a related study done in United State of America to assess the views of parents of children with sickle cell disease on preimplantation genetic diagnosis [14]. IVF with preimplantation genetic diagnosis is another reproduction alternative for reducing the risk for giving birth to children with SCD among at risk couple and this also requires assisted reproduction technology just as IVF with donor gamete [12]. The awareness as found in this study is also lower than the awareness reported by Attia and colleagues still in United States of America following another related study that evaluated the awareness and attitudes towards preimplantation genetic testing for SCD among

parents of children with SCD [15]. However, a slightly lower awareness (2.7%) was found by Mba and colleagues in Enugu, Nigeria following a similar related study done to assess awareness and acceptability of *in vitro* fertilization with preimplantation genetic diagnosis as a reproduction alternative for couples carrying the sickle cell gene [16]. These discrepancies in awareness may be explained by variation in efficiency of health information dissemination infrastructure across the different study settings. Of all the respondents' characteristics, only marital status and duration of marriage were found to be significantly associated with awareness of IVF with donor gamete as reproduction alternative for reducing the risk for giving birth to children with SCD among the respondents. This appears in line with logical reasoning as those with sickle cell trait (SCT) and married to spouses with SCT are more likely to seek for information about alternative reproduction options for reducing the risk for giving birth to children with SCD of which IVF with donor gamete is one of them. It also logically follows that the longer the duration of the marriage between couples with SCT the more likely they will have searched for information about alternative reproduction options for reducing the risk for giving birth to children with SCD.

Even after education on invitro fertilization with donor gamete as reproduction alternative for reducing the risk for giving birth to children with SCD among at risk parents only 34.2% of respondents indicated willingness to accept the option. This was however higher than 2 out of 18 respondents (11.1%) reported by Schultz and colleagues [12] to have accepted IVF with donor gamete as reproduction alternative for reducing the risk for giving birth to children with SCD. The relatively higher acceptability in our study compared to report by Schultz and colleagues may have to do with the fact that some of the respondents in their study who rejected IVF with donor gamete were noted to have reported that using the IVF with donor gamete was like working so hard to have a child who is partially genetically unrelated to the parents. On the other hand, the acceptability as found in our study was lower than that reported by Dabari and colleagues (100% for respondents that wanted more children) as well as Attia and colleagues (91% for respondents that wanted more children) in their respective related studies that assessed awareness and acceptability of preimplantation genetic testing for SCD among parents of children with SCD [14,15]. The acceptability was also less than that reported by Mba and colleagues (80.8%) in Enugu, Nigeria following a similar related study done to assess awareness and acceptability of *in vitro* fertilization with preimplantation genetic diagnosis as a reproduction alternative for couples carrying the sickle cell gene. The lower acceptability of IVF with donor gamete as reproduction alternative for reducing the risk for giving birth to children with SCD compared to IVF with preimplantation genetic diagnosis as found in above studies may be because IVF with preimplantation genetic diagnosis makes use of only the gametes from couples involved unlike IVF with donor gamete where a donor gamete has to be used hence the resulting offspring is partially genetically unrelated to the parents. To lend credence to this, Mba and colleagues reported that desire for biological children was the dominant reason for acceptance of IVF with preimplantation genetic diagnosis as reproduction alternative for reducing the risk for giving birth to children with SCD [16].

Interestingly the commonest reason given by the respondents for both acceptance (30.1%) and non-acceptance (54.8%) of IVF with donor gamete as reproduction alternative for reducing the risk for giving birth to children with SCD was their desire for biological children. The explanation for this may be that the respondents who indicated willingness to accept the option on the basis of desire for biological children must have considered using one gamete from either them or their partner and then a donor gamete from someone who do not have sickle cell trait. The offspring from such is at least partially genetically related to the couple. More still, if the couple used the male gamete of the male partner and then a donor female gamete the paternal genetic lineage is preserved. Also, since the female partner is the one to carry the pregnancy following embryo transfer and ultimately deliver the baby just as any other woman when the baby is mature it will take a genetic test to question whether the woman is the biological mother or not. There is hardly any need to prove that the mother of a child is anyone other than the one that gave birth to the child.

On the other hand, the respondents that rejected the option on the basis of desire for biological children may have been influenced by the fact that the use of donor gamete makes the resultant offspring only partially genetically related to the parents.

Of all the respondent characteristics only the Christian denomination of the respondents was found to be significantly associated with acceptability of IVF with donor gamete as reproduction alternative for reducing the risk for giving birth to children with SCD. This is not surprising since one's Christian denomination will contribute a lot in shaping one's beliefs which ultimately will influence acceptance or otherwise of IVF with donor gamete.

5. Conclusion

Both the awareness and acceptability of IVF with donor gamete as reproduction alternative for reducing the risk for giving birth to children with SCD were poor despite the challenges of raising children with SCD. To improve on both awareness and acceptance of the option, media organizations, government agencies, religious groups as well as not for

profit organizations can join forces to drive the needed change especially considering the life-long nature as well as morbidity and mortality associated with SCD.

Compliance with ethical standards

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Disclosure of conflict of interest

The author declares that there is no conflict of interest.

Statement of ethical approval

Ethical clearance for the study was obtained from the ethics committee of ESUT Teaching Hospital Parklane Enugu, Enugu State Nigeria

Statement of informed consent

The author declare that written informed consent was obtained from all the respondents.

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