Research Paper: Postpartum Depression and Physical Activity Among Women Attending Postnatal Clinics in a Tertiary Hospital in Nigeria

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ABSTRACT

Background: The reproductive years come with their own share of mental health issues with childbirth and the postpartum period being a particularly vulnerable time for mothers leading to an increase in the risk of depressive disorders. Postpartum depression has a huge public health effect on the mother with long-term consequences on the child and family. Research has shown that physical activity is beneficial; however, such studies are lacking in Nigeria. Therefore, this study sought to look at the association between postpartum depression and physical activity and determine its prevalence among women in a tertiary hospital in Nigeria.

Methods: This cross-sectional study was conducted among 401 women attending immunization and postnatal clinics at the University College Hospital Ibadan. The data were collected using a self-administered questionnaire containing a self-developed socio-demographic section, Edinburgh postnatal depression scale to measure postpartum depression, and an International physical activity questionnaire (short type) to as sess physical activity. Analysis was done using the Chi-square test and multivariate analysis to determine independent factors. Significance was set at 0.05.

Results: More than a third of the respondents (37.8%) had postpartum depression. Physical activity level was high (72.1%). High levels of physical activity increased the odds of postpartum depression compared to lower levels (95% CI=0.797-0.97). Gender of the child, marital relationship satisfaction, and age of the child were independently associated with postpartum depression.

Conclusion: This study showed that the prevalence of postpartum depression is greater than previously reported in past studies in southwest Nigeria and high levels of physical activity may increase the risk of postpartum depression.

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1. Introduction



mong all common mental health disorders, depression is the most common illness affecting people and by the year 2020, it was expected to be the second most prevalent health problem world-

wide [1]. In 2017, the World Health Organisation estimated that about 9% of the over 320 million people living with depressive disorders were in Africa [2]. Among women of reproductive age, depressive disorders lead universally. Due to the greater prevalence of depression among females compared to males, maternal mental health has become a vital public health issue and poses a challenge across the globe. The most common mental health challenge Post-childbirth is Postpartum Depression (PPD), an overwhelming illness that impairs maternal behavior [3]. PPD is classified as a major depressive episode that begins within 4 or 6 weeks of childbirth by the Diagnostic and Statistical Manual of Mental Disorders and 10th edition of the International Classification of Diseases, respectively [4]. Although the onset must be within 4-6 weeks, it is believed that women remain exposed to the risk of PPD even up to 14 months after delivery [5, 6].

It has been reported that it affects around 1 in 10 women at some time in the first year [7], studies have shown a diverse and higher range of PPD prevalence. Norhayati et al. in a review of the literature reported a prevalence of about 0% to almost 60% from one continent to another [3], while Hahn-Holbrook et al. in a large meta-analysis reported a global prevalence of 17.7% [8]. A literature review on lower-middle-income countries has placed the prevalence of PPD at approximately 20% [9]. According to studies conducted in Nigeria, about 10%-30% of women attending primary care have PPD [10]. However, Abiodun in a similar population reported a prevalence of 18.6% in developing societies [11].

Several psychological, biological, and social factors have been fingered in the etiology of PPD and have shown positive association. Psychosocial risk factors, such as a history of depression, poor relationship with spouse, weak social support, stressful periods/events prior to birth, poor social status, the stress of childcare, and complications during birth have been strongly associated with PPD [3, 4, 12]. General treatment of PPD includes medication and psychotherapy. Side effects of these drugs however are relatively unknown, especially as it relates to its effects in breast milk [13, 14] coupled with reports on relapse and other adverse effects [15]. Hence non-pharmacologic approaches are highly recommended given maternal reluctance.

In Nigeria, not every mother can afford the drugs, or the cost of psychotherapy given the socioeconomic terrain, whereas physical activity is easily accessible, affordable, and has fewer side effects. Considering the effect of PPD, physical activity should be considered and encouraged. As reported by Kołomańska-Bogucka and Mazur-Bialy in a review of the literature, physical activity is an important part of preventing PPD [16]. Furthermore, studies have shown that participation in some forms of physical activity (leisure time activity or moderate to vigorous activity) improves PPD symptoms [17-20]. However, there is a dearth of such research in Nigeria. To the best of my knowledge, no study has explored the relationship between physical activity and PPD in Nigeria, prompting this study whose main objectives were to determine the prevalence of PPD and the relationship between physical activity and PPD. Other objectives included determining other risk factors in PPD.

2. Methods

Participants

This cross-section study was carried out at the University College Hospital, which is a multidisciplinary tertiary hospital in Ibadan attending to a mix of patients from all over. The target population of the study was infant nursing mothers that came for immunization at the child welfare clinic of the Institute of Child Health and Postnatal Clinic at the University College Hospital, Ibadan. Mothers who had a delivery within the 12 months preceding this study, who were at least four weeks post-delivery were included. Women who were pregnant were excluded.

Study design

The total sampling method was employed for this study. This was due to the number of women attending the child welfare and postnatal clinics, which was about 300 women per month, and the study duration, which was scheduled for six weeks. All consenting respondents available during the six weeks duration of this study were surveyed until the required study size was achieved. The study sample size was determined using the Leslie Kish Formula 1:

$$l. n = \frac{Z\alpha^2 p q}{d^2}$$

Where, P=30.6%, q=69.4%, Z α =standard normal deviate corresponding to 95% confidence interval, critical value of 1.96, and d=0.05.

Using a previously reported prevalence of 30.6% in a Nigerian study [21], the sample size was calculated to

be 326. Using a 10% anticipated non-response rate, the sample size was rounded up to 400. In totality, 401 women participated in the study.

Data collection

The questionnaire, which was filled by the respondents was in English language and consisted of three sections.

A) Socio-demographic section: containing personal information (age, religion, tribe, educational status, marital status, family type, employment status, and occupation), family and social history (number of children, ever lost a child, help with the child, relationship satisfaction, agreement with the partner on finance, decision making, and finance), child and obstetric history (age of the present child, illness during pregnancy, mode of delivery, desired gender, complications during pregnancy, and history of depression).

B) The Edinburgh Postnatal Depression Scale (EPDS): The scale, which consists of 10 questions, asks the respondent how they have been feeling over the last one week. Responses are ranked from 0 to 3, according to severity, with an overall score of 30. This study used a score of 10 as its cut-off for PPD. This score has been suggested for the detection of mild depression [22]. As reported by Adewuya et al., "at a cut-off score of 10, the EPDS was found to be the best for screening for both major and minor depression (sensitivity= 0.867, specificity= 0.915, and diagnostic likelihood ratio for a positive result= 10.200)" [22].

C) International Physical Activity Questionnaire-SF (IPAO): It consists of seven questions that measure individuals' past 7-day levels of physical activity. This scale measures the various intensities of physical activity that people do as part of their daily activities and time spent sitting and estimates total physical activity in Metabolic Equivalent of Task (MET) per min/week and estimates sitting time. The types of activity assessed were walking, moderately intense activities, and vigorous activities. The categorical scoring method classifies physical activity into low, moderate, or high according to the number of hours and days spent in moderate or vigorous physical activities and walking. The examples of physical activities given in the IPAQ were fine-tuned to reflect activities that are common to this environment and were validated by a content expert (physiotherapy department). The activities were chosen from the compendium of physical activities and had the same metabolic equivalent of the task as the original activities given. Categorical scoring was graded as:

Low-no activity: some activities are reported but not enough to meet categories 2 or 3.

Moderate: any of the following three criteria: three or more days of vigorous activity for at least 20 minutes per day or five or more days of moderate-intensity activity and/or walking of for least 30 minutes per day or five or more days of any combination of walking, moderateintensity, or vigorous-intensity activities achieving a minimum of at least 600 MET-minutes/week.

High: any one of the following two criteria: Vigorousintensity activity for at least three days and accumulating at least 1500 MET-minutes/week or seven or more days of any combination of walking, moderate- or vigorousintensity activities accumulating at least 3000 MET-minutes/week" (http://www.ipaq.ki.se).

IPAQ has shown to be appropriate for use in developed or developing countries and has good evidence of testretest reliability [23].

Data analysis

Data were analyzed using SPSS version 20. Data collected at the end of each day was checked for errors and cleaned. Questionnaires with missing data were discarded. A research assistant was present to help with any difficulties the respondents encountered. Data were categorized into women with EPDS scores above 10 as having symptoms of depression and below 10 as not having depressive symptoms. Physical activity was categorized as low, moderate, or high.

Descriptive statistics, such as frequencies and percentages were used to summarize and present the prevalence of PPD, PA, and risk factors, such as demographic, family, obstetric, and maternal variables. Relationship satisfaction was determined from three questions, which were picked from the couple satisfaction index; 'in general, how often do you think things are going on well between you and your partner?, do you feel like a team with your partner?, and does your partner meet your needs'? Responses were ranked on a Likert scale of 0-5 and summed up to 15. Relationship satisfaction was categorized as poor (0-5), moderate (6-10), and good (11-15). The Chi-square test was used to determine the association between PPD (dependent variable) and physical activity (independent variable). Bivariate analysis was also performed to explore risk factors (independent variables) that were significantly associated with PPD at a significance level of 10%. Logistic regression was performed for all significant variables from the bivariate analysis to determine the odds ratio and 95%CI at a significance level of 5%.

3. Results

From a total of 600 women proposed to participate, 401 women willingly participated. Almost half of the women (43.1%) were within the age range of 30-34, while about 27% were above 35 years. The Mean±SD age of respondents was 31.8±4.1, with the age range of 20-50 years. Most were Yoruba (88%), the dominant ethnic tribe of Southwest, Christian (84%), and tertiary education (79.6%). Three-quarters of the respondents had less than two children (76.5%), and 32.9% had a child aged between three months and six months. Half had some sort of childcare support and almost all had their desired gender at birth (86.3%) and were in monogamous marriages (83.3%). Most of the respondents agreed with their partners on major decisions (87.3%), issues concerning finances (88%), and in-laws (79.8%). Also, most of the respondents reported satisfaction with their relationship with their partners (85.8%). Two-third of the respondents were healthy during pregnancy (78.6%), while almost all had no complications at birth (92.5%). About 59.7% of respondents had a normal delivery and less than 10% had a medical history of depression (Table 1).

Prevalence of postpartum depression and physical activity

The prevalence of PPD was 37.8%. The Mean±SD PPD score was 8.15 ± 4.7 with scores ranging from 0-26. Suicidal ideation was reported by 31 women (7.7%) who answered above 1 to the tenth question of the EPDS scale. Physical activity was generally high. Among the women, 41.2% had moderate levels of physical activity and 30.9% had higher levels of physical activity. In general, 72.1% of respondents were physically active, while 27.9% had low/no physical activity.

Postpartum depression and physical activity

There was no statistically significant association between PPD and physical activity (P=0.327), but those with higher physical activity had an increased risk of having PPD (OR= 1.255, 95%CI= 0.797-0.977) (Table 2).

Postpartum depression and other variables

Family type (P<0.001), age of the child (P= 0.025), number of children living (P= 0.019), and desired gender (P= 0.026) were statistically associated with PPD. Maternal age (P= 0.912), support for childcare (P= 0.220), previously lost a child (P= 0.413), and marital status (P= 0.156) were not statistically associated with PPD (Table 2). Medical history of depression pre-pregnancy was significantly associated with PPD (P= 0.086). Agreement with the partner on family finances (P=0.026), ways to deal with in-laws (P=0.008), decision-making (P=0.008), and marital relationship satisfaction (P<0.001) were also significantly associated with PPD (Table 3).

Multiple regression

High physical activity increased the odds of PPD compared to low physical activity (OR= 1.14; 95%CI= 0.625-2.096), but this was not statistically significant. Age of child was statistically associated with PPD. Mothers with a child aged between 6 weeks and 3 months were independently associated with PPD (OR= 0.24; 95%CI= 0.06-0.89). Women with children aged between 6 and weeks 3 months were at less risk of PPD than women with children aged older than nine months. The family type had a statistically independent significant association with PPD.

Women who were in polygamous marriages were three times more likely to have PPD than those that were in the monogamous family (OR= 3.49; 95%CI= 1.83-6.65) and single parents were less likely (OR= 0.66; 95%CI= 0.14-3.06). Women who reported having the desired gender were also less likely (OR= 0.47; 95%CI= 0.24-0.93) to report PPD symptoms than those who did not have their desired gender. Relationship satisfaction was independently associated with PPD (OR= 2.664; 95%CI= 1.317-5.390). Those with poor/ moderate relationship satisfaction were twice as likely to have PPD than those in a good relationship with a partner (Table 4).

4. Discussion

This study showed a high prevalence (37.8%) of PPD, which is comparable to some other Nigerian studies done in a similar hospital setting [21-24]. In Nigeria, varying rates from 10- 44% have been reported from different regions of the country [22, 25-27]. This wide range of prevalence is also reflected in Africa as well as other continents [28]. However, the majority of developing countries have a higher estimated prevalence than that found in high-income countries [3, 29, 30]. This variability from country to country could be due to study design (diagnostic tool, cut-off scores, and period of assessment), cross-cultural differences, socio-economic terrain, and perception of PPD/ mental health. This further indicates that a woman's susceptibility to PPD is not based on geographical location but on social, economic, psychological, and biological factors that thrive in enabling environments.

With three-quarters of the women reporting moderate to high physical activity, the prevalence of physical

Variables		No. (%)
Mother's age	<25 25-29 30-34	11(2.7) 106(26.4) 173(43.1)
	≥35 Christian	111(27.7) 337(84)
Religion	Islam Others	63(15.7) 1(0.3)
Ethnic group	Yoruba Igbo Others*	354(88.3) 20(4.8) 27(6.9)
Educational status	Primary Secondary Tertiary Others	1(0.2) 29(7.20) 319(79.6) 52(13)
Marital status	Single Married	6(1.5) 395(98.5)
Family type	Monogamous Polygamous Single parenting	334(83.3) 54(13.5) 13(3.2)
Employment status	Employed Unemployed	355(88.5) 46(11.5)
Number of children living	Less than two children More than two children	307(76.5) 94(23.5)
Age of present child	Less than 6 weeks 7 weeks-3 months >3 months-6 months >6 months-9 months >9 months-12 months	94(23.4) 99(24.7) 132(32.9) 61(15.3) 15(3.7)
Previously lost a child	Yes No	28(6.9) 373(93.0)
Had support for childcare	Yes No	203(50.6) 198(49.4)
Had the desired gender at birth	Yes No	348(86.8) 53(13.2)

Table 1. Descriptive data for socio-demographic factors (n= 401)

Variables		No. (%)
Arromont with portposing moling moles decisions	Yes	352(87.8)
Agreement with partner in making major decisions	No	49(12.2)
According to with a martine concerning family finances	Yes	354(88.3)
Agreement with a partner concerning family finances	No	47(11.7)
arrooment with partner in ways of dealing with in Jawa	Yes	322(80.3)
Agreement with partner in ways of dealing with in-laws	No	79(19.7)
	Poor	6(1.5)
Level of relationship satisfaction	Moderate	49(12.2)
	Good	346(86.3)
Illness during pregnancy	Yes	85(21.2)
	No	316(78.8)
Complications at birth	Yes	30(7.5)
	No	371(92.5)
	Vagina	235(57.9)
Mode of delivery	C/S	164(40.6)
	Forceps	2(1.5)
Medical history of depression pre-pregnancy	Yes	30(7.5)
	No	371(92.5)

Others include Edo, Hausa, Delta; < (less than), > (greater than), \ge (greater than or equal to)

activity was quite high (72.1%). Although there was no exact study measuring physical activity in postpartum women in Nigeria, two Nigerian studies reported 79% [31] and 52.2% [32] of postnatal exercises engagement with activity participation differing from this study. Other foreign studies have shown lower physical activity levels [18, 33]. High levels of physical activity in this study could be due to the economic terrain, which necessitates a woman getting back to work shortly after while joggling home care, and also because a one-year study duration was used. Physical activity was found to be lesser in the immediate postpartum period and increased constantly throughout the postpartum period. This may also have influenced the high rate reported. The increasing levels of physical activity down the postpartum period may reflect the reduction in help and support earlier received and more women being comfortable participating in physical activity. This was similarly reported by Borodulin et al. [34]. Women think it unsafe to participate in physical activity earlier than three months postpartum [32].

There was no statistically significant association between PPD and physical activity levels in this study. This

Table 2. Association between postpartum depression and physical activity
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Variables	PPD, No. (%)			05%(0)	
Physical Activity*	Yes	No	Unadj OR	95%Cl	Р
Physical activity	116(40.1)	173 (59.9)			
Low physical activity	39(34.8)	73(65.2)	1.255	0.797-0.97	0.327

*Physical activity included high and moderate scores.

Variables –		PPD (≥10		
		Yes	No	Р
Maternal age	<25 25-29 30-34 ≥35	4(34.6) 38(35.8) 69(39.9) 44(39.6)	7(63.6) 68(64.2) 104(60.1) 67(60.4)	0.912
Education	Secondary Tertiary Others	14(48.3) 121(37.9) 20(38.5)	15(51.7) 198(62.1) 32(61.5)	0.540
Employment	Employed Unemployed	138(38.9) 17(37)	217(61.1) 29(63)	0.802
Family type	Polygamous Monogamous Single parenting	34(63) 115(34.4) 6(46.2)	20(37) 219(65.6) 7(53.8)	0.000*
Religion	Christian Islam	124(36.8) 30(47.6)	213(63.2) 33(52.4)	0.105
Marital status	Married Single	4(66.7) 151(38.2)	2(33.3) 244(61.8)	0.156
Had support for child	Yes No	72(35.6) 82(41.6)	130(64.4) 115(58.4)	0.220
Number of children living	Less than 2 More than 2	109(35.5) 46(48.9)	198(64.5) 48(51.1)	0.019*
Have you previously lost a child	Yes No	14(53.8) 231(61.9)	12(46.2) 142(38.1)	0.413
Age of present child	<6weeks 6weeks-3mths >3mths-6mths >6mths-9mths >9mths-12mths	33(35.1) 29(29.3) 59(44.7) 24(39.3) 10(66.7)	61(64.9) 70(70.7) 73(55.3) 37(60.7) 5(33.3)	0.025*
Had Desired child gender	Yes No	72(20.8) 18(34.6)	274(79.2) 34(65.4)	0.026*
Illness during pregnancy	Yes No	39(46.4) 121(38.4)	45(53.6) 194(61.6)	0.183
Mode of delivery	Yes No	91(39.2) 61(37.4)	141(60.8) 102(62.6)	0.717

Table 3. Association between Postpartum depression and socio-demographic factors

Variables		PPD (≥10	Р	
		Yes	No	P
Complication at birth	Yes	15(50)	15(50)	0.176
	No	138(37.5)	230(62.5)	0.170
Medical history of de-	Yes	15(53.6)	13(46.4)	0.086
pression pre-pregnancy	No	137(37.2)	231(62.8)	0.080
Agreement with your	Yes	128(36.3)	225(63.7)	0.026*
partner concerning fam- ily finances	No	24(53.3)	21(46.7)	0.026
Agreement with your	Yes	112(35)	208(65)	0.008*
partner in ways of deal- ing with in-laws	No	40(51.3)	38(48.7)	0.008
Agreement with partner in decision making	Yes	128(36.6)	222(63.4)	0.000*
	No	24(50)	24(50)	0.008*
Relationship satisfaction	Poor/ moderate	33(63.5)	19(36.5)	0.0001*
	Good	118(34.2)	226(65.7)	0.0001*

*Significant level of 0.01

was similarly reported by Daley et al. and Saligheh, et al. [7, 35]. The latter was a cross-sectional study assessing physical activity and PPD amongst women from postpuerperal to the first-year post-delivery, similar to this present study. Other studies however reported exercise to be effective in preventing and treating mild to moderate depression [19, 20, 36-39]. These studies were either experimental or a review of the literature. Although there was no significant association, high physical activity increased the chances of developing PPD symptoms compared to lower levels of physical activity. This finding is buttressed by Demissie et al. who reported women who had high levels of physical activity had twice the risk of developing elevated depressive symptoms [18]. High physical activity in this study involved vigorous exercises, which were household activities and walking than activities performed for leisure. It has been reported that leisure/outdoor physical activity reduces PPD compared to activities due to childcare or household work [18, 40].

Age of child, which is illustrative of the postpartum period was significantly associated with PPD. Mothers with younger babies were less likely to have PPD compared to older babies. This finding is similar to that of Saligheh et al. and Shorey et al. [35, 41]. Shorey et al. who reviewed the literature using healthy women noted a general increasing prevalence with the age of the child. Age of child, which is a proxy for the postpartum period, was associated with an increase in the prevalence of PPD as the period progresses. Bugdayci, et al. reported that

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PPD prevalence increased from 29% (0-2 months) to 36% (7-12 months) and higher above 13 months [42]. This increase in PPD may account for higher outcomes of PPD in later postpartum periods than earlier ones [2, 43]. With the significant waning of physical, financial, and emotional support from friends and family coupled with the mother's full participation in home activities, childcare, employment, and/or business, one might see how this could account for increased PPD.

Most studies have found a positive association between relationship satisfaction and PPD, and this study was not any different. Whilst marital satisfaction has been suggested as a mild predictor of PPD, its effect is majorly based on the perceived level of physical, financial, and emotional support the woman receives in the relationship [3, 44, 45]. This same perceived satisfaction can be connected to the effect family setting has on PPD. In this study, the family setting was independently associated with PPD with polygamy conferring a three-fold increase in PPD than women in monogamous marriage. This finding is similarly reported in other studies done in traditional societies [45, 46]. In contrast, Ghosh and Goswami and Rahman et al. found that women coming from nuclear families suffer more from PPD [47, 48]. The quality of the relationship with the husband and the type of support received could determine the impact of family setting on postpartum symptoms.

Varial	ble	Adjusted OR	95%CI	Р
	<6weeks	0.310	0.085- 1.128	0.050*
	6wks-3mths'	0.248	0.069-0.892	0.033*
Child age	3mths-6mths	0.450	0.130- 1.561	0.208
	6mths-9mths	0.438	0.120- 1.599	0.211
	>9months	1		0.143
	Polygamy	3.491	1.832- 6.650	0.000*
Family type	Single parenting	0.660	0.143- 3.067	0.594
	Monogamy	1		0.001*
	Yes	0.466	0.237-0.916	0.027*
Desired gender	No	1		
	Poor/moderate	2.776		
Relationship satisfaction	Good	1	1.366- 5.642	0.005*
	Low	1		0.232
Physical activity	Moderate	0.728	0.412-1.288	0.276
, ,	High	1.144	0.625-2.096	0.663
Do you agree with your	Yes	1.289		
partner concerning fam- ily finances	No	1	0.562-2.956	0.549
Do you agree with your				
partner in making major	Yes	0.583	0.274-1.240	0.161
decisions	No	1		
Do you agree with partner in dealing with in-laws	Yes	0.931	0.479-1.808	0.832
	No	1		
Number of children	<2	0.640	0.378- 1.083	0.097
living	>2	1	0.370- 1.005	0.037
Medical history of	Yes	1.492	0.640.0.647	0.201
depression	No	1	0.610-3.647	0.381

Table 4. Multivariate analysis

*Significance set at 0.05

Gender of the child was a positive risk factor for PPD. This is similar to other studies done both in Nigeria [11] and other traditional societies [44, 49] where the husband's or even the wife's disappointment with the gender of the baby is significantly associated with developing PPD, specifically if the baby is a girl. This is especially seen if the woman already had a female child. Most Africans have this preference for male children as heirs and progenitors of the family put pressure on the woman. Comparably, in some western studies, a similar relationship did not exist between the gender of the child and PPD [29, 50].

5. Conclusion

PPD is prevalent here in Nigeria and is generally higher than the speculated 10%-15%. It is a global health issue that should be taken seriously as it cuts across both low- and high-income countries and associated factors are dependent upon cultural and socio-economic terrain. It is no longer a myth that can be swept under the carpet but should be openly addressed and necessary systems put in place, especially in tertiary hospitals that attends to a mix of mothers in the society, in other to enable healthier, happier families. This study hopes to encourage further research in this direction.

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Limitations

A standard scale was not used to assess relationship satisfaction; therefore, the results should be interpreted with caution. Also, as a cross-sectional study, I could not determine the temporal association between PPD and physical activity. The study population was a mix of people, the sample population may not reflect this diversity as most were educated, consequently, a generalization must be carefully made.

Ethical Considerations

Compliance with ethical guidelines

Approval for the study was sought from the University of Ibadan / University College Hospital Health Research Ethics Committee (UI/UCH/EC/16/0103). Permission was also sought from the authorities of the immunization clinic (Institute of child health, UCH) and postnatal clinic (obstetrics and gynecology department, UCH), where the study was carried out. Written informed consent was obtained from respondents after informing them of the purpose, intent, voluntary participation, and non-maleficence of the survey. Confidentiality was maintained in the questionnaire by keeping them anonymous.

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Authors' contributions

All authors equally contributed to preparing this article.

Conflict of interest

The authors declared no conflict of interest.

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