

1 **Clinical experiences with the use of oxytocin injection by healthcare providers in a**
2 **South-Western State Nigeria: A Cross sectional study.**

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25 **Abstract**

26 **Background:** Post-Partum Hemorrhage (PPH), is a leading cause of maternal mortality in
27 Nigeria and most low and middle income countries(LMIC). The World Health
28 Organization(WHO) strongly recommends oxytocin as effective, affordable and the safest
29 drug of first choice in the prevention and treatment of PPH in the third stage of labor.
30 However, there are concerns about its quality. Very high prevalence of poor-quality oxytocin,
31 especially in Africa and Asia has been reported in literature. Excessive and inappropriate use
32 is also common with oxytocin in low-resource settings.

33 **Objective:** To assess clinical experiences with quality of oxytocin used by healthcare
34 providers in Lagos State Nigeria.

35 **Methods:** It was a descriptive cross-sectional study done in 2017. Seven hundred and five
36 respondents (doctors and nurses) who use oxytocin for obstetrics and gynaecological
37 services were recruited from 195 health facilities (public and registered private) across
38 Lagos State. Data collection was quantitative, using a pretested self-administered
39 questionnaire. Data analysis was done using IBM SPSS version 21. Statistical significance
40 was set at 5%($p < 0.05$). Ethical approval was obtained from Lagos University Teaching
41 Hospital Health Research Ethics Committee. Funding support was provided by the Promoting
42 the Quality of Medicines, a program funded by the U.S. Agency for International
43 Development and implemented by the U.S. Pharmacopeia Convention.

44 **Results:** Only 52 percent of the respondents knew oxytocin should be stored at 2°C to 8°C.
45 About 80% of the respondents used oxytocin for augmentation of labor; 68% for induction of
46 labor, 51% for stimulation of labor and 78% for management of PPH. Forty-one percent used
47 20IU and as much as 10% used 30IU to 60IU for management of PPH. About 13% of the
48 respondents have experienced use of an ineffective brand of oxytocin in their practice. Just

49 over a third (36%) of the respondents had an available means of documenting or reporting
50 perceived ineffectiveness of drugs in their facility. Of these, only about 12% had
51 pharmacovigilance forms available in their facilities to report the ineffectiveness.

52 **Conclusion:** The inappropriate and inconsistent use of oxytocin especially overdosing likely
53 led to the spuriously high perception of medicine effectiveness among respondents. This is
54 also coupled with lack of suspicion of medicine ineffectiveness by clinicians as a possible
55 root cause of poor treatment response or disease progression. Poor knowledge of oxytocin
56 storage and consequent poor storage practices could have contributed to the ineffectiveness
57 reported by some respondents. There is need for the establishment of a unified protocol for
58 oxytocin use with strict compliance to the guidelines. Continued training of healthcare
59 providers in medicines safety monitoring is advocated.

60 **Key Words:** Oxytocin, clinical-experiences, oxytocin-quality, healthcare-providers,
61 Pharmacovigilance and Lagos State.

62

63 **Background**

64 Poor maternal and child health indices have remained a recurring public health challenge in
65 Nigeria. Obstetric haemorrhage especially post-partum haemorrhage (PPH) is a leading cause
66 of maternal mortality in Nigeria [1,2]. According to the world health organisation (WHO)
67 post-partum haemorrhage (PPH) is defined as a blood loss of 500 ml or more within 24 hours
68 after birth and it is said to affect approximately 2% of all women who give birth [2]. PPH is
69 associated with nearly one quarter of all maternal deaths globally[2]. In 2015 Nigeria and
70 India accounted for approximately 58,000 maternal deaths, which is over one third of the
71 global maternal deaths[3]. Fortunately, deaths from PPH are preventable. WHO strongly

72 recommends Oxytocin as an effective, affordable and the safest drug of choice in the
73 prevention and treatment of PPH[2]. Oxytocin is also used intrapartum for induction,
74 stimulation and augmentation of labour when medically indicated and where benefit
75 outweighs the risk[4,5]. Oxytocin is named one of the 13 life-saving commodities by the UN
76 Commission within the continuum of care to effectively address the avoidable causes of
77 death during pregnancy and childbirth[6]and is included in the WHO Model List of Essential
78 Medicines[7].

79 However, there are concerns about the quality of oxytocin available. Oxytocin requires stable
80 cold chain from the point of manufacture to point of use to maintain its quality[8]. It is
81 recommended to be stored in the refrigerator at 2° to 8° Celsius while some have extended
82 storage up to 20° and 25°C within a few days”[8]. A major problem of oxytocin relates to
83 heat-related degradation, inappropriate storage in the supply chain and at the health facilities.
84 In most low-income countries these storage conditions are usually very difficult to
85 maintain[9,10]. Surveillance studies have shown high prevalence of poor-quality oxytocin,
86 particularly in Africa and Asia.[10–12] Most common problems were insufficient or no
87 active ingredient[10,11]. Safe medicines supply is fundamental to public health[13]. Poor-
88 quality medicines have the greatest potential for harming the health of consumers, with far-
89 reaching consequences, which include: treatment failure, adverse drug reactions, economic
90 hardship, health problems, and death[13]. Poor quality uterotonics in circulation have dire
91 consequences. Apart from increased maternal mortality, It could also lead to performing
92 surgical procedures that could have been prevented[14].

93 In a recent study in Nigeria, the quality audit of oxytocin injections in circulation showed an
94 alarming failure rate, up 74% of sampled oxytocin injection failed quality test[10]. Despite
95 this evidence and concerns around poor-quality medicines, epidemiologic data around quality

96 of medicines is still spare and poor. Many healthcare providers again, do not generally
97 suspect medicines as a cause of disease progression and a contributor to treatment outcome.
98 Reports have it that obstetricians in Sub-Saharan Africa often give three vials of oxytocin to
99 ensure they get equivalent of at least one dose as prevention of PPH with one vial of oxytocin
100 is difficult.[14] This study serves as a sequel to the quality audit of oxytocin injections in
101 Nigeria and seeks to assess the clinical experience of health care providers in Lagos State
102 Nigeria with the quality of oxytocin injection used. It tried to assess what healthcare
103 providers know about oxytocin injection, how they use it, what their clinical experiences
104 were with use and their perceived effectiveness or ineffectiveness of the medicines.
105 Effectiveness of oxytocin in this study is the ability of the oxytocin injection used, to achieve
106 the desired contraction within the recommended dose for a specific indication.

107

108 **Materials and methods**

109 **Study population:**

110 A descriptive cross-sectional study was carried out to assess the clinical experience of
111 healthcare providers in Lagos State on the use of oxytocin. The study population consisted of
112 practicing doctors and nurses working in either public or private facilities in Lagos State. To
113 participate in the study, respondents have to be employed in registered public or private
114 health facilities in Lagos State that offered obstetrics and gynaecological services and use
115 oxytocin in their practice.

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117

118 **Sample size determination**

119 The sample size was determined using Cochran's formula considering the following criteria:
120 standard normal deviate at 95% confidence interval; 5% accepted error of margin and
121 proportion of reported effectiveness(52.5%) of another uterotonic from a previous study in
122 Nigeria[15].

$$123 \quad n = \frac{z^2 pq}{e^2},$$

124 where:

125 n = minimum required sample size

126 z = standard normal deviate a 95% confidence interval = 1.96

127 e = accepted error of margin = 5%

128 p = proportion of reported effectiveness of misoprostol from a previous study in
129 Nigeria²⁰ = 52.5%

130 $q = 1 - p$

131 thereby:

$$132 \quad n = \frac{(1.96)^2(0.525)(0.475)}{(0.05)^2}$$

$$133 \quad n = 384$$

134 Making provisions for a 30-percent nonresponse rate (to a self-administered questionnaire),
135 the minimum calculated sample size will be 499.

136

137 **Sampling Technique and Selection of Respondents**

138 Multistage sampling was used to select public and private healthcare facilities from each of
139 the five administrative divisions in Lagos State.

140 **Stage 1: Selection of Local Government Areas (LGAs) from the five**
141 **administrative divisions.**

142 A simple random sampling with ballot paper was used to select four LGAs from Ikeja
143 administrative division; two LGAs from Badagry; two from Lagos Island; one LGA from
144 Epe and one LGA from Ikorodu. This amounted to 10 LGAs from a total of 20 LGAs in
145 Lagos State.

146 **Stage 2: Selection of public and private facilities**

147 The three tertiary health facilities that provide obstetrics and gynecological services in Lagos
148 State were purposively selected. Every secondary level public healthcare facility/general
149 hospital and comprehensive primary healthcare centre (PHC) in the selected LGAs was
150 included for recruiting respondents from the public health sector.

151 **Stage 3: Selection of the private health facilities**

152 Using the list of registered private hospitals per LGA as provided by the Lagos State Ministry
153 of Health, 15 registered private healthcare facilities that offer obstetrics and gynaecology
154 services were selected by systematic sampling per LGA. This came to a total of 150 private
155 health facilities from the 10 LGAs.

156 **Stage 4: Selection of healthcare providers**

157 All registered doctors and nurses in the health facilities selected who met the inclusion
158 criteria and signed the informed consent form confirming willingness to participate were
159 included. To ensure representation, based on the proportion of doctors to nurses in the public

160 and private sector according to the Human Resources for Health indices in Lagos State, 60
161 percent of respondents recruited in the study were from the private health sector, and 40
162 percent were from the public health sector. The doctor-to-nurse ratio of 1:2 was used to
163 recruit respondents from both the public and private sectors.

164 Overall, seven hundred and five(705) respondents (doctors and nurses) who use oxytocin
165 were recruited from 195 health facilities, which included from the public sector - 3 tertiary
166 facilities; 10 General hospitals; 32 Comprehensive Primary Health Care facilities and private
167 sector - 150 private health facilities across the 5 administrative divisions of Lagos State. This
168 is shown in Table 1.

169 **Table 1: Sampling technique**

Stage of sampling	Activity	No. of samples
Stage 1	Selection of LGAs from the 5 administrative divisions in Lagos State	- 10 LGAs selected
Stage 2	Selection of public health facilities	- 3 Tertiary health facilities - 10 General hospitals - 32 Comprehensive Primary health centers(PHCs)
Stage 3	Selection of private health facilities	- 150 private health facilities
Stage 4	Selection of healthcare providers	- Doctor to Nurse ratio per facility used was 1:2

170 Table 1 gives a description of every stage of sampling technique.

171

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173

174 **Data collection technique and management**

175 Quantitative data was collected using a pretested self-administered questionnaire which was
176 developed following a literature review and incorporated expert contributions, reviews, and
177 opinions. The questionnaire was pretested among 20 clinicians (doctors and nurses) who met
178 the inclusion criteria and were from facilities in the LGAs not selected for this study. The
179 questionnaire sought information on sociodemographic characteristics of respondents and
180 occupational history of respondents; general obstetric knowledge; clinical experience with
181 Oxytocin use. The main outcome measures were proportion of healthcare providers with
182 good knowledge of oxytocin storage, pattern of oxytocin usage and dosing by healthcare
183 providers, the proportion of oxytocin perceived to be effective and ineffective by healthcare
184 providers and proportion of healthcare providers who document or take action concerning
185 perceived ineffectiveness of oxytocin in their clinical practice. Data entry, cleaning and
186 analysis were done using IBM Statistical Package for Social Sciences (SPSS) version 21.
187 Data was presented in frequency tables, simple proportions and inferential statistics was done
188 with chi-square and statistical significance set at $p < 0.05$. The mean and standard deviation
189 were used to summarize quantitative variables that were normally distributed, while median
190 and interquartile ranges (IQRs) were used for those that were found not to be normally
191 distributed. Since the responses in the study were self-reported, there was possibility of recall
192 bias and social desirability bias. However, setting the respondents recall period to the past
193 one(1) year helped minimize recall bias. Many options were offered on each question for
194 respondents to choose from and also the questionnaire is self-administered without
195 respondent's personal details(anonymity), these will reduce chances of social desirability
196 bias. In addition, every respondent who participated in this study only had a few minutes to

197 fill in the questionnaires. The questionnaires were not sent in advance hence no time to
198 prepare for the ‘apparently correct’ answer, the questionnaire clearers stated that there were
199 no right or wrong answers, they study only wanted to assess the current practice. Again
200 because it was a self-administered questionnaire, there was also the possibility of none
201 response bias, which was minimized here by almost doubling the minimum calculated sample
202 size. Ethical approval was obtained from the Health Research and Ethics Committee – Lagos
203 University Teaching Hospital, Lagos Nigeria (HREC assigned no.
204 ADM/DCST/HREC/APP/1800). Formal consent was obtained from each respondent.

205

206 Results

207 Seven hundred and five(705) respondents were participated in the study. Table 2 gives the
208 socio-demographic characteristics of the respondents. They were mostly in within the 30 to
209 40 years age bracket (41.4%) with a mean age of 36.3 ± 10.4 . There were more females
210 (71.6%) and nurses (61.0%). More respondents came from the private sector (62.1%).
211 Majority of the respondent had ten years or less working experience (64.5%) with a median
212 of 7.5years. Nearly all of the respondents (92.9%) had received some form of training on
213 oxytocin.

214 **Table 2: Socio-demographic characteristics of respondents (n=705)**

Characteristic	Category	Frequency	Percent
Age group (years)*	<20	2	0.3
	20–29	195	27.7
	30–39	292	41.4
	40–49	124	17.6
	50–59	66	9.4

	≥60	26	3.6
Sex	Males	200	28.4
	Females	505	71.6
Years of practice [†]	1–10	455	64.5
	11–20	146	20.7
	21–30	73	10.4
	≥31	31	4.4
Cadre of health worker	Doctor	275	39.0
	Nurse	430	61.0
Sector of practice	Public	267	37.8
	Private	438	62.1
Training on oxytocin use	Yes	655	92.9
	No	50	7.1

* Mean 36.3, SD ± 10.4

† Median 7.5, IQR (4, 15)

215 Table 3 gives the general obstetrics knowledge and practice of the respondent. Most of the
 216 respondent knew the correct definition of PPH (86.2%). Just over half (52.2%) of the
 217 respondents knew the proper storage place for oxytocin i.e. in the refrigerator at 2-8°C while
 218 as much as 42% stored their oxytocin on the shelves. Analysis of the indications for use of
 219 oxytocin among respondents showed that 80% of the respondents used oxytocin for
 220 Augmentation of labour, 78.2 % for Management of PPH, 68% for Induction of labour while
 221 50.6% used it for stimulation of labour as shown in figure 1. Figure 2 shows the respondents
 222 understanding of the proper storage conditions.

223 **Table 3: General obstetrics knowledge and practice of the respondents (n=705)**

Aspect	Question	Frequency (%)
Knowledge of PPH	Correct definition(Yes)	608 (86.2)
Respondents use of oxytocin in obstetrics	Stimulation of labor (Yes)	357 (50.6)
	Augmentation of labor (Yes)	564 (80.0)
	Induction of labor (Yes)	479 (67.9)
	Management of PPH (Yes)	551 (78.2)
Storage of oxytocin	Fridge	368 (52.2)
	Shelve	297 (42.1)
	Dark	30 (4.3)
	Others	10 (1.4)

224 Table 3 assessed respondents' knowledge of definition of post-partum haemorrhage, their knowledge
 225 of the recommended storage for oxytocin and what they use for in their practice.

226 More doctors (59.3%) than nurses (47.7%) correctly knew that oxytocin should be stored in
 227 the refrigerator and as well more respondents in government facilities (68.4%) than in private
 228 facilities (40.2%) knew the proper storage of oxytocin as shown in table 4.

229 **Table 4: Assessment of knowledge of oxytocin storage by Cadre and Sector of practice**
 230 **of respondents.**

Question	Frequency, N=705(%)	
	Doctors, n=275 (%)	Nurses, n=430 (%)
Storage of oxytocin		
Refrigerator	163 (59.3)	205 (47.7)
Shelves	93 (33.8)	204 (47.4)
Dark	14 (5.1)	16 (3.7)
Others	5 (1.8)	5 (1.2)
Storage of oxytocin	Public, n=267 (%)	Private, n=438 (%)
Refrigerator	182 (68.4)	176 (40.2)
Shelves	66 (24.8)	217 (49.5)
Dark place	3 (1.1)	27 (6.2)
Others	16 (6.0)	18 (4.1)

231 Table 4 further presents the analysis of the assessment of respondents' knowledge of
 232 recommended storage place for oxytocin by healthcare provider cadre and by sector of
 233 practice.

234 Twenty-three percent of the respondents monitored the effectiveness of oxytocin using the
 235 frequency and duration of uterine contraction while 65% uses frequency/duration of uterine
 236 contractions and cervical dilatation as shown in table 5.

237 **Table 5: Respondents' general practice with oxytocin (n=705)**

Questions	Response	Frequency (%)
Cadre administering oxytocin	Doctors	165 (23.4)
	Nurses	46 (6.6)
	Both	494 (70.0)
Responsibility for procurement of oxytocin	Clients	95 (13.5)
	Facility	610 (86.5)
Indicator for monitoring effectiveness of oxytocin in labor	Correct frequency and duration of uterine contractions	165 (23.4)
	Cervical dilatation	73 (10.4)
	Both of the above	461 (65.4)
	None of the above	3 (0.4)
	Others	3 (0.4)

238 Table 5 shows the cadre administering oxytocin in respondents' clinical practices, who
 239 procures and their indicator for monitoring effectiveness of oxytocin used during labor.

240 Table 6 summarizes the respondent's indication for use and dosage of oxytocin for various
 241 obstetric indications. About 48% of the respondents indicated they use 10IU of oxytocin for
 242 stimulation/augmentation of labour in primigravida, 24% use 5IU, 17% use 20IU, while 2.4%
 243 use other doses ranging from 30IU to 60IU. About forty-percent of the respondents use 5IU
 244 for stimulation/augmentation of labour in multiparas, 41% use 10IU, 10% use 20IU and as
 245 much as 4.4% use other doses ranging from 30IU and 60IU. Concerning the dosing of

246 oxytocin for prevention of PPH, 41.4% of the respondents use 20IU, 33% use 10IU, 11.3%
 247 use 5IU, 4.8% use 15IU while as much 10% use doses ranging between 30IU to 60IU.

248 **Table 6: Use and dosage of oxytocin for various obstetric indications**

Dose Amount	Max dose for stimulation/ augmentation of labor in primigravida Frequency (%)	Max dose for stimulation/ augmentation of labor in multipara Frequency (%)	Dose of oxytocin for prevention of PPH Frequency (%)
5IU	169 (24.0)	280 (39.8)	80 (11.3)
10IU	339 (48.1)	292 (41.4)	230 (32.6)
15IU	57 (8.1)	32 (4.5)	34 (4.8)
20IU	123 (17.4)	70 (9.9)	291 (41.4)
Others (30IU to 60IU)	17 (2.4)	31 (4.4)	70 (9.9)

249 Table 6 shows the different doses oxytocin used by respondents for specific indicators

250 Table 7 shows that the majority of respondents in both public (41.4%) and private (52.3%)
 251 health facilities use a maximum dose of 10IU of oxytocin for stimulation/augmentation of
 252 labor in a primigravida. Similar responses were also noted for the same indication in the
 253 multipara in both public (41.4%) and private (41.1%) health facilities. The majority use a
 254 maximum dose of 20IU units of oxytocin for the prevention of PPH in both public (43.2%)
 255 and private (40.0%) health facilities.

256 **Table 7: Use and dosage of oxytocin for various obstetric indications according to**
 257 **respondent's Sector of practice.**

	Dose Amount	Max dose for stimulation/ augmentation of labor in primigravida Frequency (%)	Max dose for stimulation/ augmentation of labor in multipara Frequency (%)	Dose of oxytocin for prevention of PPH Frequency (%)
Public Sector n=267	5IU	78 (29.3)	106 (39.8)	30 (11.3)
	10IU	110 (41.4)	110 (41.4)	82 (30.8)

	15IU	28 (10.5)	10 (3.8)	14 (5.3)
	20IU	47 (17.3)	32 (12.0)	115 (43.2)
	Others	4 (1.5)	7 (2.6)	26 (9.4)
Private Sector n=438	5IU	90 (20.5)	172 (39.3)	49 (11.2)
	10IU	229 (52.3)	180 (41.1)	146 (33.3)
	15IU	32 (7.3)	21 (4.8)	18 (4.1)
	20IU	73 (16.7)	38 (8.7)	175 (40.0)
	Others	14 (3.2)	27 (6.1)	50 (11.4)

258 Table 7 shows further analysis of different doses of oxytocin used by respondents per sector
 259 of practice.

260 Twelve popular brands of oxytocin were assessed in this survey. These brands were
 261 previously studied audited for quality [2]. The respondents' perception of the effectiveness
 262 and ineffectiveness of these brands vary significantly. These brands were de-identified for the
 263 purpose of this research. Table 8 gives the summary of the perception of
 264 effectiveness/ineffectiveness of these brands. Overall, 98.3% have had experiences of
 265 effectiveness with the oxytocin brands while 12.6% perceive the oxytocin brands they use
 266 were ineffective as seen in Table 9.

267 **Table 8: Experience of quality of oxytocin brands used in obstetrics practice (n=705)**

Brands de-identified	Perceived quality of the different oxytocin brands		
	Effective Frequency (%)	Ineffective Frequency (%)	Don't know Frequency (%)
A	450 (63.8)	29 (4.1)	226 (32.1)
B	430 (61.0)	17 (2.4)	258 (36.6)
C	122 (17.3)	24 (3.4)	559 (79.3)
D	602 (85.4)	38 (5.4)	65 (9.2)
E	149 (21.2)	33 (4.6)	523 (74.2)
F	65 (9.2)	22 (3.1)	618 (87.7)
G	38 (5.5)	26 (3.6)	641 (90.9)
H	48 (6.8)	17 (2.4)	640 (90.8)
I	50 (7.1)	19 (2.7)	636 (90.2)
J	31 (4.4)	18 (2.5)	656 (93.1)
K	23 (3.3)	16 (2.2)	666 (94.5)
L	38 (5.4)	0 (0.0)	667 (94.6)

268 Table 8 shows the respondents' experience of effectiveness or ineffectiveness with use of
 269 each brand of oxytocin listed however, the brands were de-identified here.

270

271 **Table 9: Overall experience of effectiveness and ineffectiveness of oxytocin brands used by**
 272 **respondents (n=705)**

Questions	Response	Frequency (%)
Perception of oxytocin quality	Effective	693 (98.3)*
	Ineffective	89 (12.6)*

273 * Multiple responses

274 Table 9 shows the pooled estimate of the effectiveness and ineffectiveness of the oxytocin
 275 brands used by the respondents.

276

277 Majority (64.3%) of the respondents have no available means in place within their facility to
 278 document and/or report experience of ineffectiveness. Of the few who have, most (61%)
 279 document it in the patient's case note, 27% in the clinical summary and 12% in the

280 pharmacovigilance form. In the event of oxytocin failure, 57 percent will resort to caesarean
 281 section, while 45.2 percent will change to another medicine, mainly misoprostol (40.1%).
 282 These results are summarized in table 10.

283 **Table 10: Practice following oxytocin use in obstetrics (n=705)**

Question	Response	Frequency (%)
Availability of means of documenting/ reporting perceived oxytocin ineffectiveness	Available	252 (35.7)
	Not available	453 (64.3)
Where respondents report/document perceived poor quality of medicines (n=453)	Case note	154 (61.1)
	Clinical summary	68 (26.9)
	Pharmacovigilance form	30 (11.9)
Actions taken by respondents when the maximum recommended dose of oxytocin fails	Doubling the dose	37 (5.2)*
	Change the medicine	319 (45.2)*
	Caesarean section	402 (57.0)*

284 * Multiple responses

285
 286 **Table 11: Association between sector, cadre, and knowledge of proper storage of**
 287 **oxytocin(Refrigerator) (n=705)**

Question	Response	Proper storage of oxytocin				
		Yes Frequency (%)	No Frequency (%)	Total	χ^2	P
Sector of practice	Government	183 (68.5)	84 (31.5)	267	757.88	<0.001
	Private	176 (40.2)	262 (59.8)	438		
Cadre of health worker	Doctor	159 (57.8)	116 (42.2)	275	713.34	<0.001
	Nurse	200 (46.5)	230 (53.5)	430		

288
 289 Table 11 shows that respondents in the public sector and doctors had significantly better
 290 knowledge of oxytocin storage (p<0.001).

291

292

293

294 Discussion

295 The healthcare system in most low income countries are weak. This situation is further
296 exacerbated when poor quality medicines are also in circulation. Our findings suggest poor
297 knowledge of oxytocin storage among the respondents. There was also inappropriate and
298 inconsistent use of oxytocin with the experience of ineffectiveness of oxytocin brands used
299 among respondents. Oxytocin is a peptide with a highly unstable structure. The biggest
300 obstacle to oxytocin quality is the storage and handling before patient use. The storage
301 condition of oxytocin has been widely reported as inappropriate[16]. Oxytocin is a heat-
302 sensitive medicine and should be kept between 2–8°C. Previous study in India documented
303 that most physicians and nurses did not know how oxytocin should be stored[17]. An
304 assessment in Nepal, found that only 8.6% of health facilities stored oxytocin in the
305 refrigerator[18]. Similarly, our study, showed that only 52% of the respondents knew that
306 oxytocin should be stored in the refrigerator while in practice this may just be much lower. A
307 further assessment of the association between good knowledge of proper storage of oxytocin
308 with sector of respondents' practice revealed that about 68% of healthcare providers in the
309 public sector and 40% in the private sector knew that oxytocin should be stored in the
310 refrigerator. This was statistically significant with $p < 0.001$. There was also a statistically
311 significant difference ($p < 0.001$) between cadre of staff and knowledge. As much as 41% of
312 doctors and 52% of nurses did not know that oxytocin should be stored in the refrigerator.

313 The therapeutic dose of oxytocin for induction, stimulation and augmentation of labor for
314 medically recommended reason is 5IU including prevention of PPH[4]. However, WHO
315 recommends 10IU (IV/IM) for prevention and treatment of PPH[2]. Most evidence-based
316 guidelines(U.K and Canada) in literature recommend a low dose oxytocin for induction and
317 augmentation[20]. Our findings revealed that different doses of oxytocin (low and high) were

318 used by healthcare providers in this study even within same facility. A very high proportion
319 of the respondents in our study used doses beyond the maximum recommended for intra-
320 partum use in primigravida and also in multiparas who obviously need lower doses. About
321 41% of the respondents used double the WHO recommended dose. Nearly 10% used doses
322 ranging between 30IU to 60IU of oxytocin. These translate to use of two to six vials for a
323 10IU vial to achieve desired result of uterine contraction. This may just be an indication of
324 failed quality, supporting the report in literature that healthcare providers in Africa often used
325 up to 3 vials to get the desired effect of one[14]. The findings in our study are similar to
326 reports from a previous study done in Karnataka, India[17]. This encourages wastage and
327 diversion of limited resources for saving lives of other women and improving maternal
328 health. It also increases the client's healthcare spending.

329 In assessing respondents' perceived effectiveness/ineffectiveness of oxytocin used in their
330 practice, overall, up to 13% of the respondents have experienced use of an ineffective brand
331 of oxytocin at one time or the other. Lack of suspicion of medicines quality by healthcare
332 providers as a possible cause of disease progression or contributor to treatment outcome may
333 have influenced this level of perceived ineffectiveness. Medicinal products are supposed to
334 protect patients and save lives hence should be 100% effective. The findings correlate with
335 the reports of high prevalence of poor-quality oxytocin samples in LMIC countries from
336 laboratory assays^[11,19]. No previous study within our search of published literature had
337 assessed healthcare provider perceived effectiveness or ineffectiveness of oxytocin used in
338 their clinical practice hence, posing a challenge in making comparisons.

339 The high level of knowledge of the correct definition of PPH is not surprising as our
340 respondents were supposedly highly skilled healthcare providers. Similarly in Ethiopia,
341 82.4% of the skilled healthcare providers defined PPH correctly[21].

342 The pattern of indications for oxytocin use is similar to the Nepal study where majority
343 (78%) of the health service providers used oxytocin for prevention and management of PPH
344 while 59% used oxytocin for augmentation and induction of labour[18]. Our study is
345 consistent with previous studies that oxytocin may be very commonly and inappropriately
346 used for induction and augmentation of labour[20,22], almost routinely used and given
347 contrary to guideline during labor in spite of good progress[23,24].

348 It was noted that majority (57%) of the respondents performed a caesarean section when the
349 maximum recommended dose of oxytocin failed, while 5.2% doubled the dose of oxytocin
350 used. Possible consequence of poor oxytocin quality as reported in previous studies could
351 result to excessive and inappropriate use of oxytocin and performing unnecessary surgical
352 procedures which could lead to avoidable complications and even death[13,14,20]. Despite
353 these experiences only about 36% of the respondents had a system in place for documenting
354 or reporting perceived ineffectiveness of drugs used. This again further support reports that
355 healthcare providers often do not suspect drug quality in the course of practice and usually do
356 not document[13].

357 It is possible that the inappropriate and inconsistent use of oxytocin—especially
358 overdosing—likely led to the spuriously high perception of medicine effectiveness among
359 respondents. This is also coupled with lack of suspicion of medicine ineffectiveness by
360 clinicians as a possible root cause of poor treatment response or disease progression. Poor
361 knowledge of oxytocin storage and consequent poor storage practices could have contributed
362 to the ineffectiveness reported by some respondents.

363

364

365 **Strength and Limitation**

366 There is dearth of published data on the perceived quality of oxytocin used by healthcare
367 providers and so this study contributed to the much needed data on this topical issue
368 especially in low and middle income countries with high maternal mortality mainly due to
369 haemorrhage. Another strength, is the representativeness of the respondents from public and
370 private sector and the involvement of all levels of the health system
371 (tertiary/secondary/primary) across Lagos State. However, the study did not include middle
372 and lower level healthcare providers such as community health officers, community health
373 extension workers or Traditional birth attendants who also use oxytocin in their practice
374 though not approved to use it at that level. There could be the issue of possible recall bias
375 since the responses were self-reported. A qualitative aspect to compliment the quantitative
376 data collected will be considered in further studies.

377 **Conclusion and recommendation**

378 This study brings to the consciousness of healthcare providers in Nigeria the possible
379 contribution of poor medicines quality to the poor maternal health risks and indices in
380 Nigeria. It further highlighted the level of pharmacovigilance in the healthcare system and by
381 extrapolation in various similar setting in the low and middle-income countries. Other
382 findings include the not so encouraging level of knowledge for proper storage conditions and
383 consequent storage practice of oxytocin and by extension the poor clinical outcomes of poor
384 quality oxytocin. These findings align with a previous quality audit of oxytocin injections in
385 Nigeria.

386 These have dire consequences. Over half of the respondent will resort to surgical procedures
387 when the administered oxytocin is ineffective. This calls for an urgent plan to put in place a
388 standard protocol to guide the practices in the storage and use of oxytocin. Proper reporting
389 channels on suspected poor quality of drugs should be improved including continued
390 education of health workers on the use of pharmacovigilance forms and ensuring availability.
391 There is need for continuous and expanded pre-service and in-service training of healthcare
392 providers to develop skills in drug safety monitoring including the suspicion of drug quality
393 in the chain of events that could possibly result in poor health outcomes.

394

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399

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Figure 1: Indications for use of oxytocin among respondents

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