Original Article

44-Year Temporal Trends and Causes of Maternal Mortality at the Lagos University Teaching Hospital, LUTH, Lagos, Nigeria (1976-2019)

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Abstract

Background: Nigeria has committed to global initiatives aimed at improving maternal and child health. Institutional audit of maternal mortality over a long period can provide useful information on the trends in maternal death and the impact of interventions. **Aim:** To evaluate the trends in annual deliveries, maternal mortality ratio and causes of maternal death at a tertiary institution in Nigeria over a period of 44 years (1976–2019). **Materials and Methods:** We conducted a temporal trend analysis of annual births, maternal deaths, maternal mortality ratio (MMR), and ranking of causes of maternal deaths at a Teaching Hospital, in Southwest Nigeria using available data from 1976 to 2019. Overall and segmental annual percent change (APC) of the observed trends were conducted using Joinpoint version 4.5.0.1 software. **Results:** Over the 44-year study period, 1323 maternal deaths occurred at approximately 30 maternal deaths per annum. There was a four-fold increase in MMR from 881/100,000 total births in 1976 to 3389.8/100,000 total births in 2019, at an average increase of 3.1% per annum. (APC: 3.1%; *P* value < 0.001). The leading causes of maternal mortality were hypertension, sepsis, haemorrhage, and abortion, which together contributed to more than 70% of maternal deaths. All the leading causes of maternal deaths except abortion had constant ranking during the study period. **Conclusion:** The four-fold increase in MMR at our hospital from 1976–2019 is worrying and may suggest that previous efforts at reducing maternal mortality in our institution did not lead to significant improvement toward the attainment of Sustainable Development Goal 3 (SDG3). The hospital increasingly managed complex cases especially the unbooked patients who were referred to the hospital as a last resort.

Keywords: *Causes of maternal death, join point, long-term trends, maternal mortality, Nigeria*

Introduction

Maternal deaths are catastrophic events with dire socio-economic, emotional, and psychological trauma to the family and society. Maternal mortality is not only reflective of the inequalities in access to health care but also the general socio-economic development of any society.[1] Recent global estimates showed that in 2017, about 295,000 maternal deaths occurred, one-fifth (67,000) of which occurred in Nigeria.[2] Though there has been a considerable reduction in the global maternal mortality ratio (MMR), towards achieving a global target of less than 70 per 100,000 live births, however, the estimates indicate that there was an increase in MMR for Nigeria from 560/100,000 live births in 2013 to 917/100,000 live births in 2017.[2,3] Variations in the rates of MMR exist across the geopolitical zones of the country with the northern regions having higher rates when compared with their southern counterparts.[4-6] This disparity is

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due to different socio-economic backgrounds and levels of implementation of healthcare strategies designed to reduce maternal deaths by various state governments. These may reflect the level of political will toward addressing the problem of maternal mortality.[7]

Before the current global initiative at reducing maternal mortality through the Sustainable Development Goals (SDG) 3.1, several previous programs such as the safe motherhood initiatives, and the millennium development goal 5 (MDG5), had been instituted to assist in reducing the burden of maternal mortality in Nigeria.[8-11] The Federal government of Nigeria has encouraged health institutions to conduct periodic reviews and surveillance to improve maternal and child health services in the Country. Research and capacity-building workshops on essential obstetric care[8,12,13] were also encouraged. Varying and poor implementation of maternal mortality reduction strategies by low- and middle-income countries (LMICs) has ensured they still contribute the largest chunk of maternal deaths globally.

Institutional maternal death can be a function of the three delay types. Type 1 delay is delay in taking a decision to seek health care. Type 2 delay is delay occasioned by poor communication to the hospital or poor intra-hospital transfer system while type 3 delay is inability to provide prompt emergency obstetric care in the hospital.[1-4] Efforts aimed at providing comprehensive emergency obstetric care at the tertiary hospital can reduce institutional maternal deaths. Maternal mortality audit is a very useful quality control measure for evaluating the standard of maternal health.[8,10-14] Long-term documentation of maternal mortality data when put together can help to unmask useful information about the patterns and trends of maternal deaths in the institution against the backgrounds of previous and current initiatives. This in turn can assist in designing future interventions. Most of the other published institutional data on maternal mortality in Nigeria and Sub-Saharan Africa were for relatively short time frames of between five and ten years and descriptive trend analysis was used. But trends are better demonstrated after considering the matured pattern over a long period of time.[16,17] Furthermore, contemporary analytic tools for monitoring trends such as the JoinPoint regression modeling enables a clearer appreciation of trends.[6,10,14,15,18-22] Therefore, we aimed to determine the pattern and trends of annual deliveries and maternal mortality at a Teaching Hospital, in Nigeria over a 44-year period (1976 to 2019), using the Joinpoint regression modeling.

Materials and Methods

This was a trend analysis of maternal deaths at a Teaching Hospital in Nigeria from January 01, 1976 to December 31, 2019. The hospital is a government-owned, tertiary hospital. The hospital receives referrals from primary and secondary private and government hospitals.

Maternal death is defined as the death of a woman while pregnant or within 42 days of delivery or termination, irrespective of the duration and site of the pregnancy from any cause related or aggravated by the pregnancy or its management but not from accidental causes.[10,22] We adopted the definition of maternal mortality ratio as the number of maternal deaths per 100,000 total births instead of the number of deaths per 100,000 live births because this was the definition used in the earlier publications from our institutions and would enable us to compare like with like.

Data sources

The data for the study (annual total birth, maternal deaths, MMR, and cause of death) for the period January 01, 1976 – December 31, 2019, was extracted from published data and departmental records. Published journal articles on maternal mortality trends from 1976-1985; 1986-1995; 2002-2006, and 2007-2019 were utilized for the study. Case files and departmental records of maternal deaths from 1996-2001 were retrieved and utilized for the study. Generally, the maternal deaths, deliveries, and total births in the hospital were identified by previous authors after reviewing all the registers at the accident and emergency department, labor ward, theatre, antenatal and post-natal wards, intensive care unit and the morbid anatomy department. The case files of the patients were retrieved from the medical records department and the clinical causes of death were determined by the authors. Annual total births were obtained from the birth register in the labor ward. Booked patients were patients that were registered for antenatal care in the hospital while un-booked patients were patients that did not register in the hospital but were referred, usually in emergency situations.

Trends analysis from 1976-2019

The annual total births, maternal deaths and maternal mortality ratio (maternal death/total births) from 1976 to 2019 that were extracted from previous studies were subjected to trends analysis using Joinpoint regression software (version 4.3.1). Poisson regression approach[23,24] with a maximum of 3 or 4 joinpoints was utilized and 4499 permutation tests was conducted for the trend.[25-27] The annual percent change (APC) of the overall and segmental trends (with its 95% confidence interval and *P* value) was then obtained. Statistically significant level was set at value of $P < 0.05$. Two-tailed

test of the hypothesis was assumed. To further smoothen the annual changes in trends, five-year MMR from 1976-2019, (1976-80, 1981-1985, 1986-1990, 1991-1995, 1996-2000, 2001-2005, 2006-2010, 2011-2015, 2016-2019) were calculated as average of the five annual MMRs.

The trend and the ranking of the clinical causes of death from 1976-2019 was also extracted from published data and medical records (1997-2001). The causes of death were divided into direct and indirect causes.

Data was entered on excel spreadsheet and imported into STATA (Statacorp, Texas USA) version 16 Statistical Software.

Ethical considerations

Ethical approval for this study was obtained from the human research and ethics committee of the Teaching Hospital (Ref. No: ADM/DCST/HREC/APP/3867). This was a retrospective review of anonymous and aggregated data with no ethical risk.

Results

Trend in annual deliveries from 1976-2019

In general, the number of deliveries in the hospital declined from 2839 in 1976 to 944 in 2019 [Figure 1 and Supplementary Table 1]. However, during this period of study, annual deliveries declined from 1976-1987 (APC-4.6%), followed by a non-statistically significant increase up to 1991, after which a strong but non-significant decline occurred through 1994. After 1994, the situation increased again up to 2011, this time with a statistically significant increase of 4% annually, after which deliveries declined again with 12% per year [Figure 2 and Supplementary Table 2].

Trend in annual maternal deaths from 1976-2019

Over the 44-year study period, 1323 maternal deaths occurred at an average of 30 maternal deaths per annum. The annual maternal deaths decreased from 25 deaths in 1976 to 16 deaths in 1984. Subsequently, the deaths continued to rise to 55 deaths in 1990. The number of annual deaths then decreased from 55 deaths in 1990 to three deaths in 2001. The maternal deaths increased from three in 2001 to a peak of 63 deaths in 2011. The maternal deaths then reduced from 56 in 2015 to 21 deaths in 2018 [Figure 1 and Supplementary Table 1]. Unbooked patients were responsible for 86.5%, 88.1% and 88.8% of maternal deaths in the periods 1986-1995, 2002-2006 and 2007-2019 respectively.

Trends analysis of annual maternal mortality ratio (1976-2019)

Four Join points were identified in 1995, 2000, 2012 and 2015 respectively. The MMR increased by 284.8% from 881/100,000 total births in 1976 to 3390/100,000 total births in 2019, at an average increase of 3.1% per annum (AAPC: 3.1%). There was an initial increase in MMR at an average of 7.5% per annum from 1976-1995 (APC = 7.5%, $P < 0.001$). Afterwards, there was a non-statistically significant decreased trend in MMR between 1995 and 2000, (APC = –10.5%, P value = 0.2). However, from 2000-2015, there were two non-statistically significant increased trends of 4.2% (from 2000-2012) and 25.8% (from 2012-2015) respectively. Subsequently, there was a 49.4% decline in MMR from 6698.6/100,000 total births in 2015 to 3389.8/100,000 total births in 2019 at an annual declining rate of 15.1% (P value < 0.001) [Figure 3 and Table 1].

The five-yearly MMR also showed more than three-folds increase from 854/100,000 total births in 1976-1980 to 3037/100,000 total births in 2012-2016 periods. Though there was a decline of about 50% from the 2304/100,000 births in 1991-1995 to 1466/100,000 births in 1996-2001 period [Figure 4].

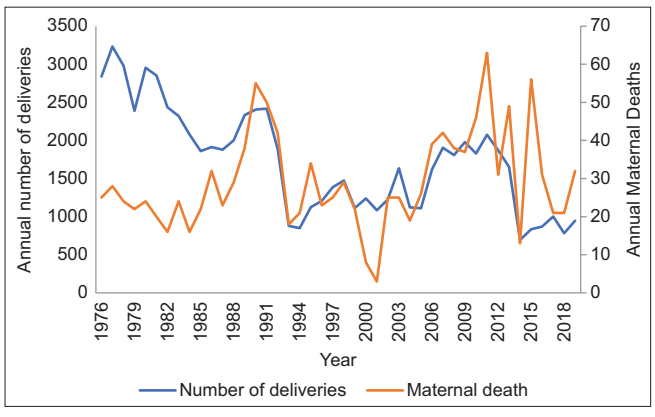

Figure 1: Trends of annual number of deliveries and maternal deaths (1976-2019)

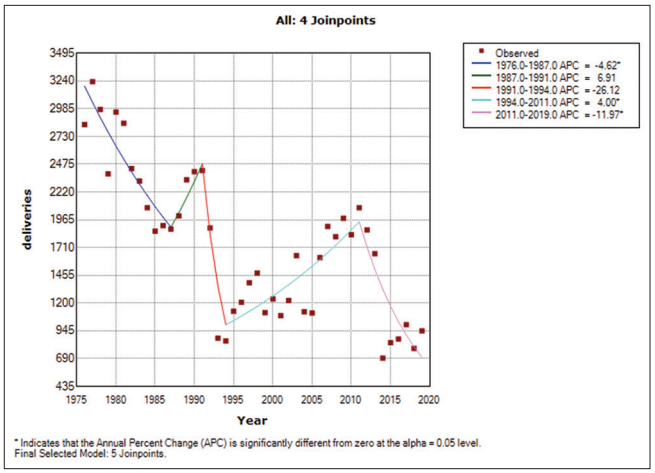

Figure 2: Joinpoint trends analysis of annual deliveries (1976-2019)

Table 1: Joinpoint estimates of the maternal mortality ratio at the Teaching Hospital in Nigeria (1976-2019)

	Trend 1 1976-1995	Trend 2 1995-2000	Trend 3 2000-2012	Trend 4 2012-2015	Trend 5 2015-2019	Overall trend 1976-2019
APC (%)	7.5	-10.5	4.2	25.8	-15.1	AAPC: 3.1
†95% CI	5.2 to 9.9	-25.9 to 8.1	-0.1 to 8.7	-27.3 to 117.8	-26.4 to – 2.0	2.1 to 4.1
P	<0.001*	0.2	0.1	0.4	<0.001	<0.0001*
Comment	Statistically Significant increase	Non-statistically significant decrease	Non-statistically Significant increase	Non-statistically significant decrease	Statistically Significant decrease	Statistically significant increase

†CI=Confidence interval, AAPC=Average annual percent change, APC=Annual percent change. *Statistical significance at $P<0.05$

Table 2: Trends in the ranking of the leading causes of maternal mortality (1976-2016)

Cause	1976-1985 (15) %, (Rank)	1986-1995 (14) %, (Rank)	1996 – 2001 %, (Rank)	2002-2006 %, (Rank) (22)	2007-2011 %, (Rank)	2012 –2016 %, (Rank)
Direct causes	85.2%	78.6%	86.3%	65%	83.8%	80.8%
Hypertension	34.8 (1st)	16.4 (2nd)	29.4 (2nd)	17.9 (1st)	27.8 (1st)	26.9 (1st)
Induced abortion	19.8 (2nd)	22.5 (1st)	-	11.2 (3rd)	10.3 (4th)	3.1 (5th)
Haemorrhage	8.6 (3rd)	11.7 (4th)	14.7 (3rd)	9.0 (6th)	14.8 (3rd)	19.8 (3rd)
Ectopic Pregnancy	8.0 (4th)	5.8 (6th)		6.0 (7th)	2.2 (10th)	2.5 (7th)
Dystocia/Uterine rupture	7.7 (5th)	8.8 (5th)	10.8 (4th)	3.0 (10th)	9.8 (5th)	3.1 (5th)
Sepsis	6.3 (6th)	13.4 (3rd)	31.4 (1st)	17.9 (1st)	18.4 (2nd)	25.4 (2nd)
Indirect Causes						
Haemoglobinopathy	3.6 (7th)	4.4 (7th)	-	6.0 (7th)	3.1 (7th)	1.0 (11th)
Other medical	2.3 (8th)		2.9 (5th)	9.6 (5th)	3.1 (7th)	8.6
HIV/AIDS	-	-	0.98 (7th)	11.2 (3rd)	4.04 (6th)	2.0 (8th
Anaesthetic	1.8 (9th)	2.0 (9th)	2.9 (5th)	1.5 (12th)	0.5 (14th)	0.5 (14th)
Anaemia	-	0.6 (11th)	4.9	5.2 (9th)	3.1 (7th)	4.1 (4th)
Cardiac + Disease	-	2.9 (8th)	1.96	-	2.2 (10th)	2.0 (8th)
Tetanus		0.9 (10th)				
Hepatic disease		0.6 (11th)				
Diabetes		0.3 (12th)				
Undetermined				1.5 (12th)		

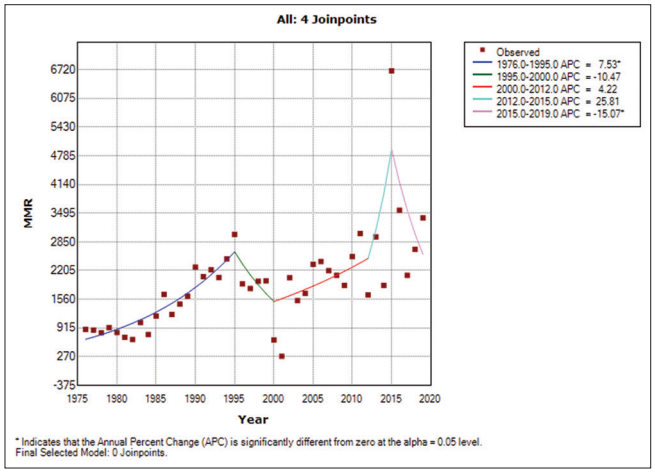

Figure 3: Joinpoint trends analysis of annual maternal mortality ratio (1976-2019)

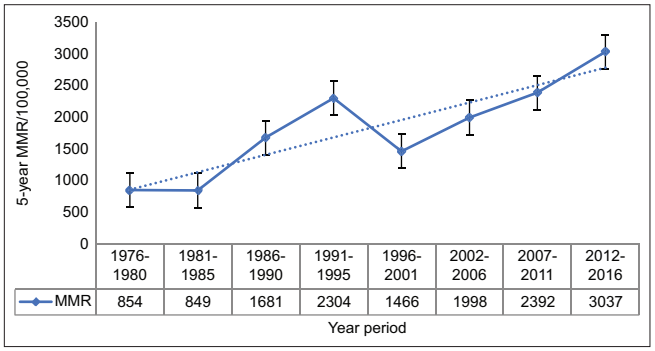

Figure 4: Trends in 5-yearly maternal mortality ratio (1976-2016)

Trends in causes of maternal mortality at the Teaching hospital (1976-2019)

Table 2 shows the trends in causes of maternal death from 1976-2019. The direct causes of maternal deaths varied in proportion from 85.2% in 1976-1985 to 65% in 2002-2006 to 80.8% in 2012-2016 [Supplementary Figure 1]. The four leading direct causes of maternal death between 1976 and 2016 were hypertension (25.5%), sepsis (18.8%), haemorrhage (13.1%), and induced abortion (11.2%) which together contributed between 69.5% in 1976-1985, and 75.2% in 2012-2016. Hypertensive disorder was the first or second leading direct cause of death during the 44-year study period. However, the contribution of hypertension to maternal mortality decreased from 34.8% in the 1976-1985 period to 26.9% in the 2012-2016 period. The contribution of sepsis increased from

the sixth-ranked (6.3%) in the 1976-1985 period to become the leading or second leading cause of maternal death over a period of 17 years from 1999-2016, recently contributing about one-quarter (25.4%) of all maternal deaths during the period 2012-2016. Except for the periods 1986-1995 (4th) and 2002-2006 (6th)), haemorrhage had maintained the third most frequent cause of maternal death during the period of the study the most recent contribution of haemorrhage to maternal deaths being 19.8% during 2012-2016 period. Notably, induced abortion declined in ranking from being the leading cause of maternal death (22.5%) in 1986-1995 to being the fifth (3.1%) during period of 2012-2016. The contribution of ectopic pregnancy also reduced from 8% in 1976-1985 to 2.5% during the 2012-2016 period.

For indirect causes of maternal death, Table 2 showed that the proportion of indirect maternal deaths has increased from 17.5% in the 1976-1985 period to 35% in 2002-2006 (largely on account of HIV/AIDS (11.2%)) and declined to 19.2% in 2012-2016 period. Haemoglobinopathy was the leading indirect cause of maternal mortality and its contributions to maternal deaths increased from 3.6% in 1976-1985 to 6.0% in the 2002-2006 period. The proportion of deaths from haemoglobinopathy then declined to 1.0% of maternal deaths in the 2012-2016 period. HIV/AIDS was first noted as an indirect cause of maternal mortality at our center in the 1996-2001 period contributing 0.98% of maternal deaths. The contribution of HIV/AID peaked at 11.2% in the 2002-2006 period and later declined to 4.0% and 2% during the periods 2007-2011 and 2012-2016 respectively. Anaemia and cardiac diseases were other leading indirect causes of maternal death.

Discussion

We reviewed the trends of the causes and rates of maternal mortality over a 44-year period (1976-2019), at a tertiary health facility in Nigeria using Joinpoint regression modelling.

Summary of main findings

The annual deliveries at our center declined from 2839 births in 1976 to 944 births in 2019 at an annual rate of 2.1% per annum. The annual number of maternal deaths however increased over the study period. The annual MMR quadrupled over the 44-year study period increasing from 881 per 100,000 total births in 1976 to 3389.8 per 100,000 total births in 2019, at a rate of 3.1% per annum. Five Join-point segmental MMR trends were identified, and the last segment showed a decline of 15.1% per annum achieving a 49.4% drop in MMR from 6698.6/100,000 total births in 2015 to 3389.8/100,000 total births in 2019.

Direct causes accounted for more than 80% of maternal deaths with the leading causes being hypertension, sepsis, haemorrhage, and induced abortion. Hypertensive disorders were either the first or second leading cause of death throughout the 44-year study period but its contribution to maternal death decreased from about 35% to about 27% over time. The contribution of sepsis increased from the sixth ranked in 1976-1985 period to be the leading or second leading cause of maternal death in the 17-year period from 1999-2016. Haemorrhage had maintained the third most frequent cause of maternal deaths for most of the study period. Induced abortion declined from being the leading cause of maternal death (22.5%) in 1986-1995 to being the fifth ranked (contributing 3.1%) during the latest period of 2012-2016.

The proportion of indirect maternal deaths increased slightly from 17.5% in 1976 – 1985 to 19.2% in 2012-2016 period. Haemoglobinopathy was previously the leading indirect cause of maternal mortality, but its contributions to maternal deaths had declined from 6.0% in 2002-2006 to 1.0% in 2012-2016 period. HIV/AIDS was first noted as an indirect cause of maternal mortality at our center in 1996-2001 period contributing 0.98% of maternal deaths. The contribution of HIV/AID peaked at 11.2% in 2002-2006 period and later declined to 2% during 2012-2016 periods.

Total births, maternal deaths, and maternal mortality trends

The present study is unique because it covered over four decades of mortality trends in contrast to most other studies in Nigeria that covered between 5 and 10 years.[4,6,10,14,15,19,28-33] This makes comparison of our findings somewhat difficult.

The annual delivery declined from about 3000 in 1976 to about 1000 in 2019 despite an increase in the estimated population in the state. Though some studies from Nigeria and elsewhere reported slight decline or stable trends in annual institutional delivery rates,[31,34,35] many studies reported an increase in annual delivery rate at tertiary hospitals in Nigeria.[6,28,29,33,36] The decline in delivery rates at our center may be due to several factors. Indeed, many private and public secondary and tertiary health facilities have been established in the state between 1976 and 2019 to improve access to healthcare in the State. The new public secondary health facilities might be more affordable and accessible to the clients. The decline in the number of deliveries might also be related to incessant strike actions by health workers of public health institutions.[14] It is also noteworthy that contraceptive prevalence in Nigeria has improved from 10% in 2012 to 19% in 2018.[37] Nonetheless, the

reduction in the annual delivery rates did not lead to reduction in the annual MMR. Indeed, the MMR (3389 per 100,000) at our center was much higher than the estimated national average MMR of about 917 per 100,000 live births (although the methods of death ascertainment are different).[2] The high institutional MMR at our center was similar to reports from other parts of the country.[19,29,32,33] However, reports from some tertiary institutions in Nigeria, the rest of Africa and elsewhere were considerably lower.[6,17,28,30,31,38-41] The observed quadrupling of MMR despite declining annual number of deliveries at our center may be because the un-booked cases that made it to our center were those critically ill patients that could not be managed elsewhere. High-risk pregnancies and complicated cases are usually referred to our center from other primary, secondary and tertiary health facilities with poor communication and referral systems. Indeed, unbooked patients contributed more than 8 out of every 10 maternal deaths that occurred. Type 3 delay within the hospital on account of inadequate facilities such as bed space, unavailability of blood and blood products, cost of health services, and consultants may not be available physically to review patients during off-hours.[1,4-12,22,28,44]

The overall significant rise in MMR at an average of 3.1% per annum over the 44-year study period suggested that the SDG-3 will not be met by 2030 unless urgent action is taken. However, the segmental trend over the last five years of the study from 2015 to 2019 offered some hope; It showed an annual MMR decline of about 15.1% per annum from 6698.6/100,000 total births in 2015 to 3389.8/100,000 total births in 2019. Some centres in Nigeria similarly reported a decline in MMR especially after introducing some initiatives into the maternity care[4,6,28,32,40] while some centres still had increasing MMR.[19,29,32,33] International comparisons showed that countries in HICs and some LMICs achieved a decline in MMR and were aiming to achieve or have achieved the SDG 3.1.[1,16,17,41] If this rate of MMR decline is maintained at our centre, it may be possible to achieve one of the targets of SDG 3 which stipulates that "by 2030, no country should have an MMR greater than 140 maternal deaths per 100,000 live births".[9,42] There is need to sustain current trends and redouble efforts aimed at reducing maternal mortality. However, to ensure a sustained institutional decline in MMR, government will need to invest more in training peripheral personnel to recognise and manage the common causes of maternal deaths and promptly refer where necessary. The government will need to increase funding for maternal health and provide subsidised health tariffs or create affordable health insurance scheme for pregnant women.[40] Infrastructures for emergency obstetric care including blood transfusion and skilled personnel should be always available. Other acute supportive care should be available in the hospital. Additionally, the initiation of strict reporting and confidential enquiry was also a reason for decline in MMR by some authors.[40,43] Thus, policies geared towards strengthening institutional response to maternal morbidity and mortality is very important in achieving SDG 3.1.[9,40,42,43]

Trends in causes of maternal mortality

We found that the leading causes of maternal deaths have remained largely unchanged over these 44 years of review. About 80% of maternal deaths were due to direct causes such as hypertension, sepsis, haemorrhage, induced abortion, uterine rupture, obstructed labour, and ectopic pregnancy. Similar pattern was reported from other centres.[4,19,21,30,31,34,35,39,44] Hypertensive disorders were the leading cause of death for most of the 44-year period. Similarly, hypertensive disorders were a major cause of maternal death in other parts of Nigeria and LMICs.[4,19,21,30,31,34,35,39,44] However, we found that the contribution of hypertensive disorders to overall maternal death at our centre decreased from 35% to 27% between 1976 and 2019. The decline in the contributions of hypertensive disorders may suggest that our centre is taking proactive steps using evidence-based protocols including the use of magnesium sulphate to reduce maternal deaths from hypertensive disorders. However, such efforts must be sustained and increased to address other leading causes of maternal death. Although, trends in causes of maternal deaths in some MICs and HICs suggested that hypertensive disorders used to be a leading cause of maternal death in the 1970's and 1980's.[45,46] However, indirect causes such as cardiac disease, pulmonary embolism, neurological conditions, drug abuse and diabetes mellitus are now the leading causes of maternal deaths in those countries.[45,47]

Sepsis increased from being the sixth ranked to become the number 1 or number 2 cause of maternal death over 17 years 1999-2016 and contributing about one-quarter (25.4%) of maternal deaths during the period of 2012-2016. Other reports also found sepsis as one of the three leading causes of maternal deaths in LMICs.[6,8,21,34,35,39] Delay in commencing antibiotics, sub-standard care, the conduct of obstetric procedures under unsterile condition, antibiotics abuse and prevalence of fake drugs probably contribute to the development of sepsis and these issues need to be tackled seriously and urgently to mitigate the contribution of sepsis as a cause of maternal mortality.[10] It is possible that the worsening socio-economic situation in the country over the years have forced health systems to

cut corners and compromise on aseptic and antiseptic measures thus resulting in high prevalence of sepsis among parturient.[14] Other predisposing factors to sepsis includes HIV infections, Diabetes mellitus, pre-labour rupture of membrane, anaemia, surgical procedures in aseptic setting with inadequate perioperative antibiotic cover.[1,2,6-10,12,14] Appropriate training of health personnel on prevention of maternal sepsis is very important. Delivery should be conducted in hygienic environment and prophylactic antibiotics should be administered where necessary. Personal hygiene and treatment of diabetes, anemia and other risk factors should be encouraged.[1,2,6-10,12,14] The finding is worrisome which is similar to recent national study.[44] Institutions should develop local Protocols for management of sepsis including a functional high dependency units and intensive care units.

Haemorrhage maintained its position as the third leading cause of maternal death for most part of the more than four decades of the study. This is in line with previous findings that haemorrhage was a leading cause of death in Nigeria, India and other LMICs.[18,29,34,39,48] Furthermore, the contribution of haemorrhage to annual maternal mortality doubled from 8.6% in 1976-1985 to 17.3% in 2007-2016 study period. Thus, efforts geared toward preventing and managing obstetric haemorrhage should be intensified. Improving the current blood banking services and offering prompt interventions that may include drugs and surgical interventions can further reduce the prevalence of haemorrhage as a cause of maternal death.

Induced abortion declined from being the second most frequent cause of maternal death (22.5%) in 1976-1985 to being the fifth (contributing 3.1%) during the period (2012-2016). It is reassuring that abortion complications have reduced as a cause of maternal mortality at our centre from 22.5% in 1976 to 3.1% in 2016. This may suggest that current initiatives such as the promotion of contraceptives among young adults, the use of manual vacuum aspirator and the use of misoprostol (medical evacuation) are yielding results.[10] There is however no room for complacency. Contraceptive prevalence in Nigeria still remains low at 17% while the unmet need for family planning is up to 48%.[49] Also the restrictive abortion laws in Nigeria may still promote clandestine and unsafe abortion with attendant complications including death.[10] Further community-based studies are warranted to confirm the current contribution of abortion complications to maternal mortality.

Back in the 1970s and 1980s, hypertensive disorders, haemorrhage and abortion complications were the leading causes of maternal deaths in the HICs similar to the current situation in LMICs. But the implementation of evidence-based interventions that were developed based on robust and systematic maternal mortality surveillance and reviews, saw a fall in MMR and a change in the leading causes of maternal deaths to indirect causes of maternal deaths such as cardiac diseases, pulmonary embolism, seizure disorders, diabetes mellitus. But these preventable causes of death still persist in our environment till date.

This study found that the leading causes or maternal death in our institution have remained essentially unchanged over this period of nearly half century. We found that overall, MMR appears to be on the rise. The leading causes of maternal death are preventable by tried and tested strategies that have worked and changed the trajectory in other LMICs and HMICs. One may then ask, why has maternal mortality in Nigeria defied solution and nothing appears to have changed? There are fundamental problems that are beyond what happens within the health facilities. The MMR will drastically reduce if Nigeria can diligently and faithfully implement recommendations to reduce the burden of maternal deaths due to hypertension, haemorrhage and sepsis. This will require a strong political will and commitment to do the needful. This is attainable if there is education and empowerment of the girlchild, free and accessible contraceptives, increased access to antenatal and delivery care, affordable health facilities with skilled birth attendants and all the signal function of emergency obstetric care, easy communications and referral systems, active systematic surveillance and review of maternal deaths and implementations of locally relevant recommendations to improve maternal health. Access to affordable healthcare remains out of reach for most Nigerians. Only 5% of the population have health insurance and 56.7% of these are male.[50,51] In 2018, out of pocket spendings on health by Nigerians was about 90% leaving the vast majority of Nigerians especially women and children vulnerable.[51]

Indirect causes contributed about 13.7%-35% (about 20% for most of the period of study) of maternal death in our study. Indirect causes of mortality generally constitute about 25% of maternal death in LMICs.[18,29,39,48] HIV/AIDS was first noted as a contributor to maternal mortality in 1996-2001 period and then peaked between 2002-2006 at 11% before its contribution declined to 2%-4% during the 2011-2016 period. Thus HIV/AIDS trends mirrored global trends.[52] The four-pronged approach of the prevention of mother to child transmission were vigorously pursued in Nigeria through international donor funds which helped to

achieve a dramatic reduction in the contributions of HIV/AIDS to maternal mortality.

Notably, malaria in pregnancy is no more a leading cause of indirect maternal death in our centre. Other studies in Nigeria also found similar drop in maternal deaths related to malaria.[4,10,28] This may be attributed to the various malaria intervention programs such as the intermittent preventive therapy and distribution of insecticide treated mosquito nets. This study indicated a reduced contribution of Sickle cell disease to maternal death. As previously noted, a unit dedicated to the management of sickle cell disease in pregnancy is now operational at our center.[53] Thus, the use of evidence-based protocol and experience in the management of such patients might have been responsible for the reduced trends.[53] Obstructed labour and uterine rupture are usually a product of poorly supervised labour, but they are still major causes of maternal deaths at our centre and elsewhere in Nigeria.[54] Deaths from ectopic pregnancy reduced from 6% in 1976 to 2.5% in 2016, possibly because of increased index of suspicion and a standing protocol of prompt interventions for all cases of ectopic pregnancy at our centre. Zero fatality from ectopic pregnancy is however achievable.

Strength and limitation

A limitation of the study is that since the research was an amalgam of different studies conducted by different authors at different times, there may be some difference in methodology utilized. Nevertheless, the documented methodologies were similar across all the periods of the study. Another limitation of the study was that there has been a slight change in the definition of MMR over time from maternal death per total delivery to maternal death per live birth. However, this study adopted the older definition to enable meaningful comparison across all the periods. A limitation of the study may also be that there might changes and improvement in the reporting and recording of maternal deaths over time which may impact on the MMR trends. However, since the studies utilized are hospital-based and not population based, therefore the changes in reporting protocol within the hospital may not affect the MMR. It is also a limitation of the study that we do not have data to evaluate the various levels of delay and to investigate other remote causes of maternal deaths. Our study is an ecological study and may not be extrapolated to other centres. Nonetheless, the strength of this study is that to our knowledge this study is the first to utilize robust Joinpoint trends analysis tool over such a long period of 44 years to evaluate and document maternal mortality trends in Nigeria.

Conclusion

The institutional MMR at our centre increased at the rate of 3.1% per annum from 1976 to 2019, despite a decline in annual birth rate. The leading causes of maternal death over the 44 years period were hypertensive disorders, sepsis and haemorrhage which together accounted for over 70% of maternal mortality. Deaths from abortion, malaria, anaemia and ectopic pregnancy reduced over the study period possibly because of public health interventions. In contrast, the pattern of the leading causes of maternal mortality in HICs has changed from hypertension, sepsis, abortion and haemorrhage to cardiac diseases, seizure disorders and pulmonary diseases over similar period following strict implementation of evidence-based protocols. It appears that the various historical and current interventions have not made much impact on the burden and causes of maternal deaths at our centre.

Although there was a downward trend in MMR of about 15.1% per annum from 2015 to 2019, more evidence-based interventions should be introduced to maintain and possibly accelerate this downward trend to achieve the SDG3 target of less than 140 deaths per 100,000 live births by 2030. Efforts aimed at developing locally relevant protocols for the prevention and management of the leading causes of maternal mortality should be sustained. It is encouraged that routine active surveillance of maternal mortality should be instituted to obtain more information to design evidence-based health system interventions. In-depth study and commitment to implement workable recommendations at all levels will assist to reverse the trends. Success of these will also depend on political commitment by central, regional and local governments to the notion that women's lives are worth saving. Furthermore, we recommend that institutional maternal audit should be encouraged and properly documented to provide evidence for improving maternal health in the country.

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Contributions of authors

JAO and GO conceptualized and designed the study protocol. HO contributed to the study design and collection of the data. AOU and JO contributed to data collection. GO analyzed the data. JAO, GO, HO and JO interpreted the data. JAO drafted the manuscript. GO, AOU, JO and HO reviewed the manuscript. All authors accepted the final version of the manuscript. JAO supervised the overall conduct of the study as part of a larger study. The author (s) read and approved the final manuscript.

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Conflicts of interest

There are no conflicts of interest.

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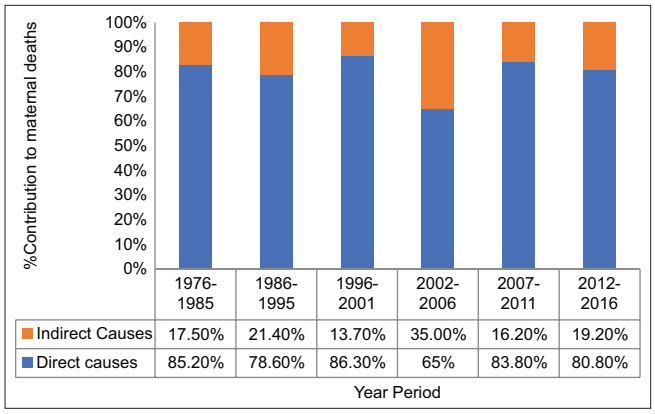
Supplementary Table 1: Overall trends in maternal mortality from 1976-2019

Year	Number of deliveries	Maternal death	Maternal mortality ratio (MMR per 100,000 total birth)
1976	2839	25	881
1977	3233	28	866
1978	2979	24	806
1979	2387	22	922
1980	2954	24	812
1981	2851	20	702
1982	2435	16	657
1983	2321	24	1034
1984	2076	16	771
1985	1860	22	1183
1986	1912	32	1670
1987	1879	23	1220
1988	2001	29	1450
1989	2332	38	1630
1990	2407	55	2280
1991	2418	50	2070
1992	1889	42	2220
1993	878	18	2050
1994	851	21	2470
1995	1124	34	3020
1996	1207	23	1905.6
1997	1387	25	1802.4
1998	1475	29	1966.1
1999	1113	22	1976.6
2000	1238	8	646.2
2001	1084	3	276.8
2002	1224	25	2042
2003	1635	25	1529
2004	1121	19	1695
2005	1109	26	2344
2006	1618	39	2410
2007	1905	42	2204.7
2008	1809	38	2100.6
2009	1978	37	1870.6
2010	1828	46	2516.4
2011	2075	63	3036.1
2012	1871	31	1656.9
2013	1654	49	2962.5
2014	695	13	1870.5
2015	836	56	6698.6
2016	870	31	3563.2
2017	1001	21	2097.9
2018	783	21	2682.0
2019	945	32	3389.8

Supplementary Table 2: Joinpoint estimates of the annual deliveries at the teaching hospital, Nigeria (1976-2019)

	Trend 1 1976-1987	Trend 2 1987-1991	Trend 3 1991-1994	Trend 4 1994-2011	Trend 5 2011-2019	Overall trend 1976-2019
APC (%)	-4.6*	6.9	-26.2	4.0*	-12.0*	AAPC: -2.1
†95% CI	-7.0 to -2.2	-12.1 to 30.1	-56.7 to 26.2	2.1 to 5.9	-16.9 to -6.7	-2.7 to – 1.5
P	<0.001*	0.5	0.3	<0.001*	< 0.001*	< 0.0001*
Comment	Statistically Significant decrease	Non-statistically significant increase	Non-Statistically Significant decrease	Statistically Significant increase	Statistically Significant decrease	Statistically significant decrease

†CI=Confidence interval, AAPC=Average annual percent change, APC=Annual percent change. *Statistical significance at *P*<0.01



Supplementary Figure 1: Trends in the percentage contribution of direct and indirect causes of maternal death (1976-2016)