Scholars Journal of Applied Medical Sciences (SJAMS) **ISSN 2320-6691 (Online)**
Sch. J. App. Med. Sci., 2015; 3(1C):198-205 **ISSN 2347-954X (Print)**

(An International Publisher for Academic and Scientific Resources)
www.saspublishers.com DOI: 10.36347/sjams.2015.v03i01.041

Research Article

Risk Factors for Primary Postpartum Hemorrhage in Benghazi, Libya: A Case Control Study

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Abstract: Primary postpartum hemorrhage (PPH) defined as blood loss in excess of 500 ml from the genital tract within the first 24 hours following vaginal delivery. PPH is a main cause of considerable maternal morbidity and mortality worldwide. The objective was to identify and quantify potential risk factors for the disease during 2009. Furthermore, to calculate the population attributable risk percentage for the most significant modifiable risk factor and to assess interaction. A hospital based case control study was done in Benghazi, Libya: 153 newly diagnosed cases of primary PPH admitted to Benghazi main hospital and an age matched group of 200 controls were randomly selected from the same hospital without PPH. Both cases and controls were subjected to a predesigned questionnaire. Significant risk factors for PPH were: previous caesarian section with OR 5.0; 95%CI(2.0-13.0), pregnancy induced hypertension with OR 4.0; 95% CI (1.8-10.6), blood transfusion after labor with OR 26.0; 95%CI (7.8-85.0), previous PPH, OR 2.6; 95% CI (1.15-6.1) posterior placenta, OR 2.0, 95% CI(1.2-3.5) and irregularity of antenatal visits with OR 2.0; 95% CI(1.18-3.7). Population attributable risk percent was calculated for modifiable risk factors and arranged in ascending manner: Regularity of booking =6%, Pregnancy induced hypertension =7%, Anaemia=13%, API (Attributable Proportion of interaction) =64%, Rothman index >3.25 indicated a synergistic effect. Adapted regular booking, management of pregnancy induced hypertension and management of anaemia could prevent postpartum haemorrhage. Education programs focusing on the modifiable risk factors are required in particular with improvements MCH services.
Keywords: Post partum hemorrhage, Potential risk factors, Hospital based, Case control, Benghazi

INTRODUCTION

Postpartum hemorrhage (PPH) is excessive bleeding from genital tract after delivery of child [1]. Primary postpartum hemorrhage defined as blood loss of 500 ml from the genital tract within the first 24 hours following delivery [2].

Postpartum hemorrhage is one of the leading causes of maternal mortality. Death due to PPH is reported to represent between 17% and 40% of maternal mortality in some parts of the world. Even in developed countries, for example USA and The Netherlands, PPH causes 13% of all recorded maternal deaths [3]. In EMRO, incidence ranged from 7.3% to 11 % and maternal mortality from 3.2 % up to 8.7% [4].

PPH usually ranks in the top of three causes of maternal mortality, along with embolism and hypertension. In the developing world, several countries have maternal mortality rates in excess of 1000 women per 100,000 live births, and World Health Organization statistics suggest that 25% of maternal deaths are due to PPH, accounting for more than 100,000 maternal deaths per year [5].

Objectives

- To identify and quantify the potential risk factors for postpartum hemorrhage in Al Jumhorya Hospital, Benghazi during 2009.
- To calculate the population attributable risk % (PAR %) for modifiable risk factors.
- To assess the potential interaction between significant risk factors subsequently to provide preventive guidelines.

METHODOLOGY

A case-control study was conducted which involved 153 subjects with postpartum hemorrhage cases with confirmed diagnosis, selected from obstetrics and gynecology department at Al-Jumhorya hospital. The control subjects, which accounted for 200, was

drawn randomly from the same hospital in obstetrics and gynecology department during 2009.

Sources of data were from patient interviews and records review; both cases and controls were matched by age, hospital and nationality. Predesigned questionnaire was adopted to collect socio-demographic characteristics that included: Age, residence, occupation of patient (house wife and others), education (low for illiterate up to preparatory and higher for other), income of family and husband smoking.

In addition, data was collected about risk factors , antenatal care, partum and post partum information including: last menstrual period, expected date of delivery, date of delivery, gravidity, parity, abortion, number of living children, last child birth, antenatal booking, regularity of booking, , specific drugs, obstetrics diseases, medical diseases, surgery, obstetric and gynecological history , blood transfusion after delivery , type of delivery ,placental site by ultra sound , status of fetus , presentation of fetus ,birth weight ,duration of admission , causes of post partum hemorrhage, previous history of post partum hemorrhage and hysterectomy.

A pilot phase was done at the beginning of the study for accuracy and reliability and completeness of questionnaire and informed consent was obtained from the study subjects

Sample size calculation

Assuming that type I error adopted at 5% and type II error at 20% (power 80%), Z at 5%=1.96 and Z at 20%=.84. We used the formula [6]:

$$N>2\ (Z\alpha+Z\beta)^2 X\ (Variance/\ MDD)^2$$

Where, MDD=minimal detectable difference.

Inclusion criteria

Age between 20 to 45years, Libyan, resident in Benghazi with term pregnancy admitted to Al-Jumhorya hospital with data about primary post partum hemorrhage.

Exclusion criteria

Preterm labor and gestational age less than 36weeks, home delivery, secondary post partum hemorrhage , none Libyan nationality, age < 20years and > 45 years and bleeding disorders.

Source of cases

Purposive sample was used to enroll cases from obstetrics and gynecology department at Al-Jumhorya hospital, include: post natal ward, post operative ward, high risk room, shock room, labor room (either normal delivery, instrumental delivery or caesarean section).

Source of the controls

Selected during full working day .they were systemically selected randomly from the same hospital in obstetrics and gynecology department, from post natal ward

All control had normal delivery without any assistance.

Matching

Cases and control were matched with age, nationality and hospital.

Measurement of exposure

Measurement in the study as following: by clinical signs of patient and quantitative methods by visual assessment (It was the main method used in obstetrics and gynecology departments at Al-Jumhorya hospital either by direct collection of blood into bedpan or plastic bags and or by number of towels socked with blood).

The collected data was handled and analyzed using SPSS software version 11.5 [7]. Fisher Exact Test (FET) was used when applicable, Level of significance < 5% was adopted. We calculated odd ratios (OR) and its correspondent 95% confidence interval for potential risk factors [8]. The (PAR %) was calculated by Bruzzi method for modifiable risk factors and Rothman Index for interaction between significant risk factors [9, 10]

RESULTS

Total number of subjects in this study was 353 comprising 153 cases and 200 controls. The study subjects collected from Al-Jumhorya Hospital, Benghazi during 2009. Cases and their controls were selected according to predefined criteria. The mean age for cases and controls was 30.3 years (SD 6.2 years) and 29.2 years (SD 6 years) respectively.

Table 1 represents the sociodemographic characteristics of cases and control subjects. Both were matched by age, nationality and hospital. The majority of control subjects were living in Benghazi represents 80.5% compared to 86.3% of the cases. Furthermore, 75% of control were house wives compared to 69.3% of cases. Low education was equally reported, also 83% of control subjects were low income compared to 79% of cases. Likewise 51.5% of control subjects, their husband smoking were positive compared to 48.4% of the cases, without significant difference observed in items of table.

Table 1: Frequency distributions of 153 cases of primary post partum hemorrhage and 200 control according to sociodemographic characteristics

Variables	Controls		Cases		Total	OR+
	N=200	(%)	N=153	(%)	N=353	(95% CI)
Age						
≤24 Yrs	53	(26.5)	28	(18.3)	81	NA
25-30 Yrs	73	(36.5)	55	(35.9)	128	
31-35 Yrs	38	(19.0)	35	(22.9)	73	
>36 Yrs	36	(18.0)	35	(22.9)	71	
Residence						
Benghazi	161	(80.5)	132	(86.3)	293	*R1*
Others	39	(19.5)	21	(13.7)	60	1.5(0.85-2.7)
Occupation						
House wife	150	(75.0)	106	(69.3)	256	*R1*
Others	50	(25.0)	47	(30.7)	97	0.8(0.47-1.2)
Education						
Low	54	(27.0)	42	(27.5)	96	*R1*
High	146	(73.0)	111	(72.5)	257	1 (0.64-1.6)
Income/monthly						
Low	166	(83.0)	121	(79.1)	287	*R1*
High	34	(17.0)	32	(20.9)	66	0.8 (0.45-1.3)
Husband smoking						
No	97	(48.5)	79	(51.6)	176	*R1*
Yes	103	(51.5)	74	(48.4)	177	0.9(0.58-1.3)

OR + Unadjusted OR, NA=Not applicable, R1=reference

Table 2: Frequency distributions of the studied cases and control subjects according to obstetric history

Variables	**Controls**		**Cases**		**Total**	**OR+**
	N=200	**(%)**	**N=153**	**(%)**	**N=353**	**(95% CI)**
Gravidity						
≤ 3	120	(60.0)	103	(67.3)	223	R_1
> 3	80	(40.0)	50	(32.7)	130	1.4(0.9-2.1)
Parity						
≤3	155	(77.5)	118	(77.1)	273	R_1
>3	45	(22.5)	35	(22.9)	80	0.9(0.6-1.6)
Abortion						
≤ 3	199	(99.5)	148	(96.7)	347	R_1
> 3	1	(0.50)	5	(3.30)	6	0.2 (0.02 -1.3)
Gestational Age						
Term	146	(73.0)	115	(75.2)	261	R_1
Post term	54	(27.0)	38	(24.8)	92	1.1 (0.7 -1.8)
Number of living children						
≤ 3	155	(77.5)	117	(76.5)	272	R_1
> 3	45	(22.5)	36	(23.5)	81	0.94 (0.57 -1.5)
Last child birth						
≤3y	169	(84.5)	129	(84.3)	298	R_1
>3y	31	(15.5)	24	(15.7)	55	0.99 (0.6-1.8)
History of PPH						
No	191	(95.5)	136	(88.9)	327	R_1
Yes	9	(4.50)	17	(11.1)	26	2.6(1.15-6.1)
History of PIH						
No	193	(96.5)	129	(84.3)	322	R_1
Yes	7	(3.5)	24	(15.7)	31	4.0 (1.8-10.6)

OR + Unadjusted OR, NA=Not applicable, R_1=Reference, H.PPH= Previous history of post partum hemorrhage, History of PIH= Pregnancy induced hypertension

Table 2 represents obstetric history of both control and cases subjects, shows that 40% control had gravidity more three times compared to 32.7% of cases, also 22.5%of control had parity more than three times compared to 22.9% of cases. Furthermore, 0.5% of the control group had abortion more than three times compared to 3.3% of cases and 27% of controls had post term pregnancy compared to 24.8% of cases group. Likewise, 22.5% of control had more than three children compared to 23.5% of cases. Controls had 15.5% of last child birth more than three years compared to 15.7% of cases.

No significant difference was reported in previous items. The previous history of post partum hemorrhage represent 4.5% of controls compared to 11.1% of cases with significance difference, OR=2.6, 95% CI (1.15-6.1). History of pregnancy induced hypertension represent 3.5% of controls compared to 15.7% of cases with significance difference, OR 4.0; 95%CI (1.8-10.6)

Table 3: Frequency distributions of cases and control subjects according to gynecological, obstetric surgery, general surgery and blood transfusion

Variables	Controls		Cases		Total	OR^{+}	OR^{++}
	N=200	(%)	N=153	(%)	N=353	(95% CI)	(95% CI)
History of curettage							
No	166	(83.0)	127	(83.0)	293	R_1	NA
Yes	34	(17.0)	26	(17.0)	60	1 (.57-1.75)	
History of myomectomy							
No	200	(100)	152	(99.3)	352	NA	NA
Yes	0	(0.0)	1	(0.70)	1		
History of Previous CS							
No	194	(97.0)	132	(86.3)	326	R_1	
Yes	6	(3.00)	21	(13.7)	27	5(2.02-3.04)	4.7(1.8-12.9)
History of Multiple CS							
No	200	(100)	146	(95.4)	346	NA	NA
Yes	0	(0.00)	7	(4.60)	7		
General surgery							
No	183	(91.5)	138	(90.2)	321	R1	NA
Yes	17	(8.50)	15	(9.80)	32	1(0.6-2.4)	
History of Blood transfusion after delivery							
No	197	(98.5)	110	(71.9)	307	R1	R1
Yes	3	(1.50)	43	(28.1)	46	26(7.8 -85)	26 (7.9-87)

CS= caesarian section, OR^{+}, OR^{++}= Unadjusted OR, NA=Not applicable, R1=Reference

Table 3 **r**epresents gynecological and obstetric surgery of control and cases ,history of curettage was reported equally in both control and cases. No control with history of myomectomy compared to 0.7% of cases without significance differences , previous caesarian section represent 3% of controls compared to 13.7% of cases with significance difference OR =5.0,CI (2.02-13.04).

No controls with history of multiple caesarean compared to 4.6%of cases with significance difference (FET=0.003). 1.5% of control subjects had blood transfusion after delivery compared to 28% of cases with significance difference, OR =26.0, 95%CI (7.8-85).

Table 4 represents the antenatal care for both cases and control subjects , shows that 18% of control had late booking compared to 20.3% of cases without significance difference and 12% of controls were irregular booking compared to 22.2% of cases with significance difference and OR=2, 95%CI (1.16-3.7).

On other hand 90.5% of control were taking drugs at booking compared to 86.3 % of cases without significance difference. Also 4% of control were taking specific drugs compared to 15% of cases with significance difference, OR=4, 95% CI (1.8-9.7)**.**

Placenta characteristics for both control and case shown that 18% of control had posterior placenta compared to 31.3% of cases with significance difference, OR=2.95% CI (1.2-3.5). No control had placenta previa compared to 3.9% of cases with significance difference FET=0.006, likewise abruptio placenta represent 6.5% of cases with significance difference FET=0.000.

Table 4: Frequency distributions of cases and control subjects according to antenatal care and placenta characteristics

Variables	Controls		Cases		Total	OR^{+}
	N=200	(%)	N=153	(%)	N=353	(95% CI)
Time of booking						
Early	164	(82.0)	122	(79.7)	286	R_1
Late	36	(18.0)	31	(20.3)	67	0.9 (.5 -1.5)
Regularity						
Irregular	24	(12.0)	34	(22.2)	58	R1
Regular	176	(88.0)	119	(77.8)	295	2.1(1.18-3.7)
Drugs in Booking						
No	19	(9.50)	21	(13.7)	40	R_1
Yes	181	(90.5)	132	(86.3)	313	1.5 (0.8-2.9)
Specific drugs						
No	192	(96.0)	130	(85.0)	322	R_1
Yes	8	(4.00)	23	(15.0)	31	4.0 (1.8 -9.8)
Site by ultrasound						
Anterior	164	(82.0)	105	(68.7)	269	R1
Posterior	36	(18.0)	48	(31.3)	84	2.0(1.2 -3.5)
Placenta Previa						
No	200	(100.)	147	(96.1)	347	FET=0.006
Yes	0	(0.00)	6	(3.90)	6	
Abruptio placenta						
No	200	(100.)	143	(93.5)	343	FET=0.000
Yes	0	(0.00)	10	(6.5)	10	

OR^{+}, OR^{++} =Unadjusted OR, NA=Not applicable, R1=Reference, FET=Fisher Exact Test

Specific drugs as antihypertensive and antithyroid drugs etc., Drugs booking include folic acid and ferrous tablets

Table 5: Frequency distributions cases and control subjects according to partum and post partum characteristics

Variables	Controls		Cases		Total	OR^{+}	OR^{++}
	N=200	(%)	N=153	(%)	N=353	(95% CI)	(95% CI)
Presentation							
Cephalic	199	(99.5)	149	(97.4)	348	R_1	NA
Breech	1	(0.5)	4	(2.6)	5	0.2 (.02-1.7)	
Number of fetus							
Single	196	(98.0)	151	(98.7)	347	R_1	NA
Twins	4	(2.0)	2	(1 .3)	6	2(.2 8 -8.52)	
Status of fetus							
Alive	199	(99.5)	146	(95.4)	345	R_1	NA
Dead	1	(0.5)	7	(4.6)	8	0.1(0.01-0.86)	
Mode of delivery							
Normal	200	(100)	105	(68.6)	305	NA	NA
Abnormal	0	(0.0)	48	(31.4)	48		
Instrumental delivery							
No	200	(100)	143	(93.5)	343	NA	NA
Yes	0	(0.0)	10	(6.5)	10		
Caesarean section							
No	200	(100)	115	(75.2)	315	NA	NA
Yes	0	(0.0)	38	(24.8)	38		
Birth weight							
$\leq$ 3.5 Kg	140	(70.0)	96	(62.7)	236	R_1	NA
> 3.5 Kg	60	(30.0)	57	(37.3)	117	0.7(.46-1.13)	

OR^{+}, OR^{++} = Unadjusted Odds Ratio, NA=Not applicable, $R_{1=}$ Reference

Table 5 represents partum and post partum characteristic of control and cases. It shows that 0.5% of controls had breech presentation compared to 2.6% of cases. Similarly 2% of control group had history of twins pregnancy compared to 1.3% of cases without significance difference. Likewise 0.5% of controls had dead fetus compared to 4.6% of cases without significance difference, OR=0.1, 95%CI (0.01-0.86).

All controls had normal delivery compared to 68.6% of cases with significance difference (FET=0.000), no controls had history of instrumental or caesarean delivery compared to 6.5% and 24.8 % of cases respectively with significance difference (FET=0.000). Likewise 30% of controls had babies with birth weight more than 3.5Kg compared to 37.3% of cases without significance difference.

Calculation of Population attributable risk percent (PAR %)

Population attributable risk percent was calculated for modifiable risk factors and arranged in ascending manner: Regularity of booking =6%, Pregnancy induced hypertension =7%. Anaemia=13%.

From preventable point of view: Adapting regular booking could prevent 6% of PPH , Likewise management of pregnancy induced hypertension could prevent 7% of PPH Furthermore, management anaemia could prevent 13% of PPH

Assessment of interaction

The parameter of interaction was done for pregnancy induced hypertension and placenta site by ultra sound. Pregnancy induced hypertension OR =4.0, Placenta site by ultra sound OR=2.0, both risk factors OR=14.0**,** RERI (Relative Excess due to Interaction) =9%, API (Attributable Proportion of interaction) =64%, Rothman index >3.25 indicating a synergistic effect.

DISCUSSION

Among 153 cases of primary postpartum hemorrhage, the present study initially found the most frequent cause of PPH was due to uterine atony, which represented 50.3% of cases followed by genital trauma in 32.7%, retained placenta in 15% and 2% represented coagulation deficit and hysterectomy was performed in 2.6% of cases. This was comparable to a study done in Pakistan ; uterine atony was reported in 64.4% and genital trauma in 34.7%, retained placenta in 7.6% and 3.3 % had coagulation deficit and hysterectomy represent 3.3 % of cases [11].

Likewise approximate findings reported from Zimbabwe [12] which agree with study in Columbia reported that uterine atony increased risk 2-4 fold [13].Uterine atony was also approved to be significant risk factor for PPH in retrospective study done in Canada [14].

On other hand, a study was carried out in California [15] showed variability of risk factors for PPH and higher rates of cases, significantly reported among obstetrical trauma and chorioamnionitis, which were not comparable to our study ,while agreement with the present study that approved no associated risk factors for PPH in relation to patient characteristics.

The present study showed that from total cases of PPH 24.8% of patients were delivered by caesarean section compared to 68.6% who delivered vaginally. This was comparable to data from New South Wales [16] but it was controversy to study performed in Ottawa, Canada, 2005 which observed that PPH rates increased due to cesarean section [17]. The present study approved increased risk of PPH among operative vaginal delivery and approximate finding was found in another study done in Canada, 2007 [18].

The present study demonstrated increased in blood transfusions in 28.1% of cases compared to 1.5% of controls. Recent study done in the United States , showed that positive relationship between severe obstetric morbidity and the use of blood transfusions and procedures to control bleeding have been used as markers of the severity of PPH [19, 20].

In Australia, Scotland and USA, increases in the reported rates of severe complications of childbirth have been almost entirely due to reported increases in the use of blood transfusions and or severe obstetric hemorrhage. In these countries it appears that not only are PPH rates increasing but so is the hemorrhage severity [21, 22]. International differences may reflect differing attitudes among obstetricians about blood transfusions.

The present study also reported that primipara and multipara did not increase risk of PPH, in agreement with study done in Jordan university [23], likewise case control studies in Saudi Arabia [24] reported that PPH carries no different risk with primipara and multipara .The present study also revealed that post term pregnancy not approved statically significant between cases and control. This was comparable to large cohort study in Denmark [25].

Pregnancy induced hypertension (PIH) was reported as one of most common risk factor for PPH in the present study. This was comparable with study performed in Norway, European countries survey on Marker for Severe maternal morbidity (MOMS-B Survey) [26, 27]. The present study revealed that irregularity of visit during antenatal care increased risk of PPH. Comparable finding with studies done in New Zealand and Nigeria [28, 29].

The present study approved that there is a significant relationship between placenta previa, abruptio placenta, uterine fibroid and increased risk of PPH. This was comparable with studies done in Australia and Tochigi Japan [30, 31]. Data from the present study also demonstrated increased risk of PPH with women who had previous caesarean section. This also approved in retrospective analysis in Saudi Arabia [32].

The present study revealed also that women with previous postpartum hemorrhage had increased risk of PPH and it was represented 11.1% among cases and 4.5% among control group. This was comparable with study done in Sydney, Australia [33].

CONCLUSION

- Causes of postpartum hemorrhage found in the present study were: Atonic uterus, genital trauma, retained placenta, coagulation deficit. The main potential significant risk factors for PPH according to their significance are: anemia before delivery, history of previous caesarean, pregnancy induced hypertension, and irregularity of antenatal visit. Others potential significant risk factors found in the present study were: previous post partum hemorrhage, fibroid and placenta previa, abruptio placenta, site of placenta**,** instrumental delivery.
- Population attributable risk percent was calculated for modifiable risk factor revealed that adapted regular booking, management of pregnancy induced hypertension and management of anaemia could prevent postpartum haemorrhage.
- The parameters of interaction were multiplicative rather than additive.

Recommendation

This study created the following recommendations:

Education programs focusing on the modifiable risk factors are required in particular with improvements MCH services including health education and promotion of antenatal care, management of anemia before delivery, management of pregnancy-induced hypertension. This only requires short time and little costs. Furthermore, well designed, large, multi centric studies are needed.

Limitations

As any case control study have in general include selection bias and recall bias and in present study: Incomplete medical files, visual estimation of blood loss was the most frequent method used to diagnosis of PPH. Disorganization of PPH cases in hospital word (no independent unit for management of PPH cases). Ultra sound was done by inexperienced person.

Strengths included: Control of confounding during design through matching of cases and control, randomization selection of control and during analysis by multivariate logistic regression, identical interview of cases and control by the same investigator.

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