

## ORIGINAL ARTICLE

**Comparison of Frequency of Postpartum Hemorrhage in Spontaneous versus Prostaglandin Induced Labour at Term Gestation**Sumaira Mubasher<sup>1</sup>, Shazia Syed<sup>1\*</sup>, Sobia Nawaz Malik<sup>2</sup>, Aisha Ishtiaq<sup>1</sup>, Humera Bilqis<sup>2</sup>, Humera Noreen<sup>2</sup>**ABSTRACT**

**Objective:** To compare the frequency of postpartum haemorrhage in spontaneous versus induced labor at term.

**Study Design:** A comparative cross-sectional study.

**Place and Duration of Study:** The study was conducted at the Department of Obstetrics and Gynecology, Benazir Bhutto Hospital Rawalpindi, Pakistan from April 2021 to March 2022.

**Methods:** A sample size of 108 women fulfilling inclusion criteria was categorized into two equal groups of 54; Group-A spontaneous onset of labor (SOL) and Group-B of induced labor with prostaglandin (IOL). Both groups were analysed for the frequency of postpartum haemorrhage PPH. Also, the association was checked by using Pearson Chi-square test of significance and t-test for comparing means. A *P*-value of  $\leq 0.05$  was considered as significant.

**Results:** The mean age of women in Group-A vs Group B was  $26.78 \pm 4.78$  years vs  $25.96 \pm 4.70$  years. Mean gestational age was  $38.33 \pm 0.97$  weeks vs  $38.72 \pm 1.02$  weeks. Multigravida (67%) were more than primigravida (33%). Postpartum haemorrhage was seen more in Group-B 24 (44.4%) compared with Group-A 11 (20.4%), with a significant *P*-value ( $P = 0.008$ ). The mean estimated blood loss (EBL) was higher in Group-B ( $675.00 \pm 420.41$  ml) than in Group-A ( $442.78 \pm 279.25$  ml) with a significant *P*-value ( $P = 0.003$ ). EBL in each group was cross checked by Haematocrit levels (%Hct) and mean value of %Hct was decreased post-delivery in women with postpartum hemorrhage. Consequently, blood transfusions were more in Group-B 16 (29.6%) than Group-A 9 (16.7%). Upon stratification for parity, the rate of PPH was higher in multigravida. The secondary maternal outcomes like; prolonged second stage of labour, uterine atony and retained placental tissues were also more in Group-B.

**Conclusion:** The induction of labor is associated with a significant risk of postpartum hemorrhage and should be offered only when it is deemed necessary.

**Keywords:** Induction of labour, Post-delivery Blood Loss, Postpartum Hemorrhage, Spontaneous onset Labour, Uterine Atony.

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**Introduction**

Obstetric hemorrhage, a preventable emergency, affects 14 million women annually, with postpartum haemorrhage (PPH) contributing to almost 25% of all maternal deaths.<sup>1</sup> Postpartum haemorrhage is unpredictable and is associated with great magnitude of maternal morbidity and mortality. All over the world, the prevalence of postpartum haemorrhage resulting in massive transfusions and

hysterectomy has increased significantly over the first decade of the new millennium, with the reported incidence being 1 in 1000 women in developing countries while 1 in 100,000 in developed or high-income countries.<sup>2</sup>

WHO defines postpartum haemorrhage as more than 500 mL of blood loss within 24 hours of a normal vaginal delivery and greater than 1000 mL after caesarean section.<sup>3</sup> Globally, postpartum haemorrhage affects about 6% of all deliveries and annually 2% of women need intensive care unit admission.<sup>4</sup> Risk factors for PPH include; multiple pregnancy, good size baby, prepartum anemia, placenta previa, maternal age >35 years, preeclampsia, and prolonged labor. A strong association of PPH has also been suggested with Caesarean section, operative vaginal delivery and induction of labor.<sup>5-7</sup> In developing countries, PPH poses a more significant concern due to constrained health resources and public awareness, maternal anemia and high parity. These factors make maternal compensation for excessive blood loss more difficult, leading to enhanced maternal morbidity and mortality.<sup>8</sup>

Induction of labour is a commonly employed obstetric intervention in a high risk pregnancy when continuation of pregnancy is hazardous for the mother, baby or for both (Standard indication).<sup>9</sup> According to international research, the average rate of Induction of labour is now as high as 20–25% of all pregnancies, owing mainly to its unjustified offering even in low risk pregnancy without any medical indication as well as due to frequent request by the mothers too, to suit their reasons and convenience (Non-Standard indications).<sup>10,11</sup>

Various pharmacological (Prostaglandins, Misoprostol, oxytocin, nitric oxide, mifepristone) and non-pharmacological methods (membrane sweeping, amniotomy, cervical catheters, extra amniotic laminaria tents) are used to induce labour. Any such intervention will alter the normal course of pregnancy and labor, increasing the risk of complications like uterine hyperstimulation, fetal distress, postpartum hemorrhage, caesarean delivery, and even uterine rupture, particularly in women with previous uterine scars.<sup>10</sup>

Literature review reveals a plethora of studies,

comparing the association of PPH with elective Induction and spontaneous onset of labor. A meta-analysis of three large multicenter trials reports a significant association between labor induction and hemorrhage in multiple studies.<sup>8,10,12,13</sup> While some recent trials and a Cochrane review reveal no such association.<sup>14-16</sup> Moreover, results of various other studies are reported to be inconsistent due to non-standardized measurements of postdelivery blood loss, insufficient statistical power when PPH is a secondary outcome, indication bias and method used for IOL.<sup>4,17-19</sup> Finally use of oxytocin during labor, prolonged labor, and operative vaginal delivery are other associated factors compounding this relationship of IOL with PPH.<sup>20,21</sup> With such conflicting background there is a continued need to further explore the relationship between induced labor and risk of PPH while excluding the compounding factors. With the same objective we designed this study to investigate whether induction of labour carries a higher risk of PPH compared with spontaneous onset of labor in low risk parturients. This study will also provide baseline data for the risk of PPH in induced labor in our population, based upon which the management strategies could be revised to optimize the rate of induced labour, thereby reducing the risk of PPH.

## Methods

The comparative cross-sectional study was conducted at the Department of Gynecology and Obstetrics of Benazir Bhutto Hospital Rawalpindi, Pakistan for one year from April 2021 to March 2022 after getting approval from the Institutional Research Forum and Hospital Ethical Committee held on dated: 31<sup>st</sup> March 2021 vide letter no: 34/IREF/RMU/2021. A sample size of 108 women (54 in each group) was calculated using a WHO sample size calculator with a Confidence Interval of 95% and Power of test 90%. Sampling technique was non-probability consecutive sampling. The inclusion criteria were; gestational age from 37 weeks to 41 weeks, Singleton cephalic Low-risk pregnancy aimed for planned vaginal delivery. The main indications for Induction of labour were; post-dated pregnancy (40+1 weeks to 41 weeks of gestation), decreased fetal movements with normal CTG, pre-labour rupture of membranes, and non-complicated

Diabetes Mellitus.

Exclusion criteria were; maternal age < 20 years and > 35 years, Grand multiparity (>5 paras), elective/emergency Caesarean and other High-risk pregnancies like; previous caesarean section/uterine Scars, previous history of postpartum hemorrhage, Assisted vaginal delivery, Pregnancy with medical disorders; hypertensive disorders, heart disease, renal disorders, Intrauterine growth restriction/Oligohydramnios, coagulopathy.

After informed written consent, labouring women from labour room fulfilling the inclusion criteria were enrolled in the study and categorized into two groups: Group-A (having women only with spontaneous onset of labor (SOL) and Group-B having women whose labour was induced (IOL). For uniformity of results, all Inductions were done with 3mg prostaglandin E2 vaginal tablet 6 hours apart up to 3 maximum doses. In both groups, labour was followed up prospectively. A partogram was maintained with vigilant feto-maternal monitoring. Labour was augmented with oxytocin when required. Women landing into emergency caesarean delivery or having assisted vaginal delivery were excluded from the study while women accomplishing vaginal delivery were assessed for postpartum hemorrhage, till the target number of 54 was achieved in each group. Intravenous oxytocin (10ml) was given only as a part of AMTSL (Active

management of the third stage of labour). All vaginal blood loss was collected in a tray fixed underneath the delivery table, and then transferred to a 500 ml kidney tray for blood loss estimation. All used gauze pieces/sponges were also weighed before and after delivery to calculate total blood loss. For verification, Hematocrit levels were measured pre and post-delivery. PPH was labelled at >500 ml of blood loss. Secondary outcome variables studied were: Prolonged Second Stage of Labor, Uterine Atony, Retained products of conception, uterine rupture, and Maternal ICU admission. All information was recorded on a specially designed Performa.

#### Statistical Analysis

Data analysis was carried out through 'The Statistical Package for Social Sciences (SPSS)', version 25.0. Mean and standard deviation were calculated for quantitative variables while qualitative variables were measured as frequency and percentage. A Chi-square test was applied to determine the frequencies of PPH and other outcomes between the two groups, while an independent sample t-test was applied to determine the significance between differences of hematocrit (hct) and mean blood loss (ml). A *P*-value of  $\leq 0.05$  was considered as significant.

#### Results

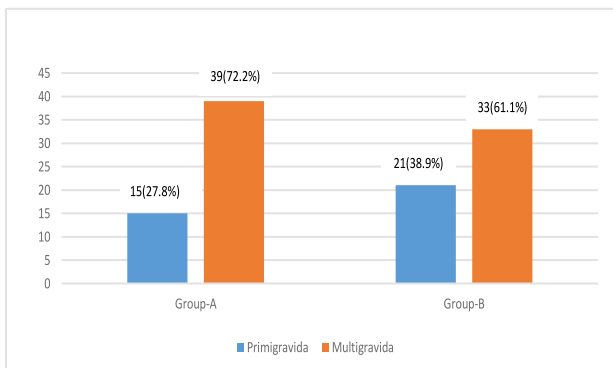
The study included a total of 108 women, divided into two groups of 54 women each; Group-A (SOL)

Parameters	Group-A (SOL) <sup>1</sup> n=54		Group-B (IOL) <sup>2</sup> n=54		P-Value
	Mean	SD	Mean	SD	
Maternal Age (years)	26.78	4.78	25.96	4.70	0.374
Gestational Age (weeks)	38.33	0.97	38.72	1.02	0.045
Pre-delivery % Hct	34.12	3.19	34.34	2.75	0.699
Post-delivery % Hct	27.45	5.67	28.16	4.91	0.710
Estimated Blood Loss(ml)	442.78	279.25	650.00	420.41	0.003
<b>Secondary Outcomes</b>	<b>Yes</b>	<b>No</b>	<b>Yes</b>	<b>No</b>	
Blood Transfusion	09	45	16	38	0.110
Second Stage of Labour > 120 min	00	54	01	53	0.315
Uterine Atony	11	43	23	31	0.013
Retained Products of Conception	10	44	14	40	0.355
Uterine Rupture	00	54	00	54	--
Maternal ICU admission	00	54	00	54	--

<sup>1</sup>Spontaneous onset of labour, <sup>2</sup>Induction of labour

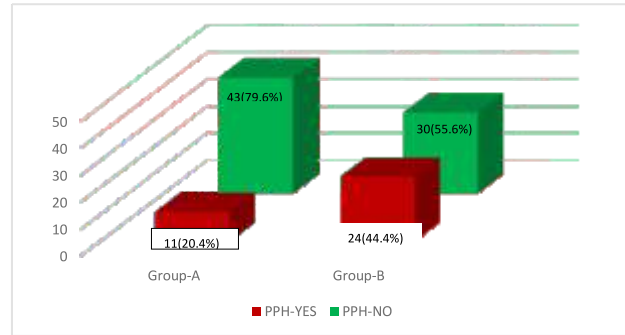
included women with spontaneous labour and Group-B (IOL) included women having induced labour with prostaglandin. The mean age of women in Group-A was  $26.78 \pm 4.78$  years and in Group-B  $25.96 \pm 4.70$  years. The mean gestational age in Group-A was  $38.33 \pm 0.97$  weeks and in Group-B  $38.72 \pm 1.02$  weeks. (Table-1).

In Group-A, 15 (27.8%) women were primigravida and 39 (72.2%) were multigravida. In Group-B, 21 (38.9%) women were primigravida and 33 (61.1%) were multigravida with *P*-value (*P* = 0.221). In both study Groups multigravida women were more than primigravida. (Figure.1).



**Fig.1: Comparison of Parity in Study Groups**

In Group-A, PPH was seen in 11 (20.4%) women while 43 (79.6%) women had no PPH. In Group-B, 24 (44.4%) women had PPH and 30 (55.6%) escaped PPH, with a significant *P*-value (*P* = 0.008). In our study, women with postpartum hemorrhage were more in Group-B than Group-A. (Figure.2). The mean value of estimated blood loss (EBL) in



**Fig.2: Prevalence of Postpartum Haemorrhage in two Groups (*P*-value=0.008)**

Group-A women was  $442.78 \pm 279.25$  ml and in Group-B was  $675.00 \pm 420.41$  ml with significant *P*-value (*P* = 0.003). The mean EBL was more in Group-B than Group-A. Table-1.

Blood loss in each group was cross-checked by Haematocrit levels (%Hct). The mean value of %Hct was decreased post-delivery in women with postpartum hemorrhage. Table-1. Consequently, blood transfusions were also more in Group-B 16 (29.6%) than Group-A 9 (16.7%). Table-1.

The results of secondary maternal outcomes showed that complications of the prolonged second stage of labour, uterine atony and retained placental tissues were more in Group-B compared to Group-A. Table-1.

No case of uterine rupture or Maternal ICU admission was seen in either group.

Upon stratification of parity for PPH, the rate of PPH was found to be higher in multigravida women. Table-2.

**Table-2: Stratification of Parity with Postpartum Haemorrhage (PPH) in Study Groups**

Parity	PPH	Group-A (SOL*) n (%)	Group-B (IOL**) n (%)	Total n (%)	<i>P</i> -Value
Primigravida	Yes	02 (13.3%)	09 (42.9%)	11 (30.6%)	0.058
	No	13 (86.7%)	12 (57.1%)	25 (69.4%)	
Multigravida	Yes	09 (23.1%)	15 (45.5%)	24 (33.3%)	0.045
	No	30 (76.9%)	18 (54.5%)	48 (66.7%)	

\*Spontaneous onset of labour, \*\*Induction of labour

**Discussion**

Labor induction is a common obstetric practice all around the world. The reported statistics for IOL in the United States are 24.5%, in Sri Lanka 35.5%, 6.8% to 33% in Europe, while this rate for Pakistan is 42%.<sup>22</sup> Such high rate of Induction may lead to PPH contributing to high maternal morbidity and

mortality. However, an association of PPH with induced labour has remained controversial, therefore we planned this study to comment upon this association in our local settings.

In our study, the mean age of women in Group-A (SOL) and Group-B (IOL) was 26.78 vs 25.96 years (*P*=0.374), and mean gestational age was 38.33 vs 38.72 weeks (*P*= 0.003). The overall frequency of PPH

in our study was 32.4%, much higher than another recent local study reporting 14% but comparable to Yasmin et al. study, Upon analysis of individual groups, the frequency of PPH was found to be 20.4% vs 44.4% in Group-A (SOL) and Group-B (IOL) respectively, with a significant  $P$ -value= 0.008.<sup>8,23</sup> These results were quite consistent with low-risk cohort study results of Rafiq et al. (7.6% vs 21.7%,  $P=0.002$ ) and Yasmin et al. (20.58 % vs 50%), indicating a higher PPH frequency in the induced labor cohort compared to spontaneous onset of labour group.<sup>8,23</sup> The latest meta-analysis reports that in women having a vaginal delivery, the risk of PPH is higher in induced versus spontaneous labour, regardless of the indication and method of induction.<sup>10</sup> A PPH of  $\geq 500$  mL or  $\geq 1000$  mL; both occurred more often in women who had IOL than those with spontaneous labour (13.3% vs. 8.6%,  $P < 0.001$  and 3.1% vs. 1.9%,  $P = 0.001$ ), respectively. This association has been studied extensively in the context to maternal parity as well. Earlier studies have reported no association between induced labour and PPH in primiparas but were lacking statistical power to analyse this outcome. Two recent local studies by Bukhari et al. and Shah et al. enrolling only primigravidas reported significantly more frequency of PPH in induced vs spontaneous labour (7% vs 44%  $P=0.03$  and 18.8% vs 38.9%  $P=0.01$ , respectively).<sup>12,13</sup> In the Rafiq et al. study, there was an overall higher frequency of PPH in primigravidas as compared with multigravidas, however, in the induced group, PPH was more in multiparas, with equivocal results in primiparas.<sup>8</sup> One explanation could be a comparatively prolonged first labour and subsequent uterine atony leading to increased risk of PPH. Upon stratification of parity for PPH, our study reveals statistically significant PPH ( $P=0.045$ ) among multiparous women. Previously mentioned few studies and a Cochrane review reports no such association between IOL and PPH in low risk pregnancies.<sup>4,14-16</sup> Nevertheless, few other randomized controlled trials reporting no evidence of a difference between outcomes of induced and spontaneous labour, had a primary focus on the mode of delivery or neonatal outcome and not the postpartum blood loss.<sup>24,25</sup> Neither, the important risk factors for haemorrhage like uterine

atony, retained placenta, or coagulopathy were taken into account for multivariate analysis, nor the amount of blood loss was cross-verified by a fall in hemoglobin levels.

The amount of blood loss is likely to be underestimated in the absence of a proper quantitative measurement method.<sup>10</sup> We opted for a proper method for post-partum blood loss estimation. The mean estimated blood loss was high in Group-B than Group-A and blood loss in each group were cross-checked by Haematocrit levels (%Hct) as well. The mean value of %Hct was decreased post-delivery in women with PPH. Consequently, blood transfusions were also more in Group-B 16 (29.6%) than Group-A 9 (16.7%). This is in contrast to the already mentioned studies where induced labour was not associated with increased blood loss after delivery.<sup>4,16</sup> In fact they reported a slight, but statistically significant, reduced decrease in hemoglobin after delivery compared to SOL. Such varied results of all studies inclusive of ours, are attributable to specific strengths and limitations of a particular study.

As far as the secondary maternal outcomes of our study are concerned, the complications of the prolonged second stage of labour, uterine atony, and retained placental tissues (RPOC's) were also encountered more in the induced group. Uterine atony, alone is responsible for up to 60-to 80% cases of PPH with approximately five times more risk of developing PPH in subsequent delivery as compared to controls.<sup>1</sup>

The phenomenon of an increased risk of PPH with the induction of labour has been explained by various hypotheses. The first culprit might be the inducing agent itself. The drug used can affect the uterine muscle directly leading to its supraphysiological contraction and fatigue, culminating in postpartum uterine atony and hence PPH. This enhanced risk might further be substantiated by the cumulative impact of prolonged or high-dose oxytocin administration on the myometrium to reduce its contractility after delivery, due to desensitization of the oxytocin receptors.<sup>26</sup> Another hypothesis is that high dosage oxytocin administration is a sign of prolonged labor, which in turn is associated with uterine atony.<sup>27</sup> The oxytocin

augmentation contributed to almost one-third of cases of PPH in few studies regardless of the method in which labour first began.<sup>10,28</sup>

The majority of our women in both groups with PPH, had their labour augmented with oxytocin.

Due to almost universal use of oxytocin in labor after an induced labour, it is difficult to adjust for this confounding variable while relating the induction of labour with PPH.

Finally, it has been suggested that the duration of the both latent and active phases of labor could be unique in women with induced labor and act as a confounding factor while determining the relation between induction of labour and PPH.<sup>10</sup> This hypothesis can explain the enhanced risk of PPH after induction of labour performed for standard indications and not for non-standard indications as most of the standard inductions are performed on an unfavorable cervix. Besides prolonged active labor, other dynamics of labour might play a role in induced labour to jeopardize the myometrial contractility soon after delivery.<sup>12</sup>

In view of all aforementioned contributory risk factors for PPH, induction of labour should be done judiciously and all such women be monitored cautiously for post-partum blood loss. To reduce maternal morbidity and mortality, it is imperative to identify the preventable causes of PPH and its sequelae. Pregnant women should be sensitized about the importance of standard antenatal care and competent birth attendants. The health service providers must be educated on better use of emergency obstetric services to avoid PPH. Nevertheless, despite good antenatal care and timely detection of preexisting health problems, PPH still cannot be avoided in the majority of cases. Our study's findings may contribute towards reducing maternal morbidity and mortality in the context of our resource-restricted health settings, where the significance of such a study becomes even more pronounced. The bias in our results was minimized by recruiting a uniform low-risk sample size in both groups and excluding women with any risk factor for PPH. The inducing agent was also the same in all women having induced labour. The main limitation was that our results could not be extrapolated to multiple gestation and caesarean deliveries, which

were excluded from the study. Moreover, our results need to be stratified according to the indication of induction and duration of labour too.

### Conclusion

The induction of labor is associated with a significant risk of postpartum hemorrhage due to multiple factors. To minimize the morbidity and mortality associated with PPH, induction of labour should be offered only where it is deemed necessary. There should be a judicious plan and indication for labor induction, supported by clear departmental Standard Operating Procedures.

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**Conflict of Interest:** The authors declare no conflict of interest

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**Authors Contribution**

**SM:** Idea conception, data collection, manuscript writing and proofreading

**SS:** Idea conception, study designing, manuscript writing and proofreading

**SNM:** Data collection, data analysis, results and interpretation

**AI:** Data collection

**HB:** Data analysis, results and interpretation

**HN:** Manuscript writing and proofreading

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