ORIGINAL RESEARCH article

Analysis of anti-hypotensive drug pattern use in the Neonatal Intensive Care Unit: A comparative study between the public and private sectors in Libya

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Abstract: Neonatal hypotension is a critical and frequent condition in the Neonatal Intensive Care Unit (NICU), often requiring pharmacologic intervention. Despite established treatment strategies, considerable variability exists in clinical practice across different healthcare settings. This study aimed to compare the neonatal characteristics, clinical practices, treatment indications, and outcomes of patients admitted to a public hospital and a private clinic in Libya. A cross-sectional comparative study was conducted from December 2024 to April 2025. Data were collected using a validated standardized questionnaire that included neonate demographics, clinical presentation, diagnostic assessment, drug use patterns, outcome, and adverse events. A total of 120 neonates were included in the study. Neonates admitted to the private NICU had significantly more favorable baseline characteristics compared to those in the public NICU. A lower measured blood pressure and higher significant use of echocardiography (p<0.001) were observed in the private NICU. Dopamine was the primary agent used in the public NICU (85.7%) while the private NICU relied on combination therapy, including dobutamine (p<0.001). Clinical response occurred more rapidly in the private NICU. Conversely, a higher rate of mortality was observed in the public NICU compared with the private NICU (p<0.001). The current findings suggest a significant disparity in diagnosis, drug selection, and outcome between public and private NICUs. Thus, establishing standardized protocols and increasing access to diagnostic tools, such as echocardiography, could enhance neonatal outcomes, particularly in resource-limited settings.

Introduction

Arterial hypotension (AH) is a common issue in neonates, with the potential to influence short- and long-term outcomes. In preterm neonates, conditions associated with cardiovascular instability and low arterial pressure often include challenges in adapting to extrauterine circulation during the first 72 hours after birth [1-3]. Other significant neonatal complications linked to arterial hypotension include sepsis, necrotizing enterocolitis,

persistent pulmonary hypertension of the neonate, perinatal asphyxia, congenital heart disease, and patent ductus arteriosus [2, 4-6]. Moreover, the intricate pathophysiology of AH in preterm infants, whether occurring during the transitional period or linked to complications of preterm birth, adds to the ongoing controversies [7]. Systemic hypotension is a common complication in preterm infants, affecting one-third of very low-birth-weight neonates. Among these, 16.0%-52.0% undergo volume expansion while 04.0%-39.0% receive vasopressor therapy [8]. Significant variability exists across neonatal units in the reported prevalence of hypotension, the thresholds for initiating treatment, and the approaches to cardiovascular support [8]. Major factors contributing to hypotension in neonates such as preterm myocardium. The immature heart of preterm neonates has a reduced ability to increase cardiac output in response to an increase in preload, compared to the mature heart. This is due to its lower contractile force and decreased compliance [9]. Neonatal cardiac myocytes are smaller and less organized than those of mature hearts, with fewer myofibrils and mitochondria. Also, they contain less intracellular calcium and rely on trans-sarcolemma calcium flux for myocardial contraction [10]. In term infants, the ductus arteriosus typically closes within 12 to 15 hours after birth. However, in preterm infants, this closure is delayed due to increased pulmonary vascular resistance linked to lung disease, reduced sensitivity of ductal tissue to oxygen, and elevated levels of circulating prostaglandin E2. A large patent ductus arteriosus leads to reduced systemic blood flow due to left-to-right shunting. Since the ductus remains open during both systole and diastole, this creates a steal syndrome, reducing diastolic blood flow to vital organs such as the kidneys and intestines [11-13]. Uterine contractions during labor cause intermittent decreases in oxygen delivery, which trigger neuroendocrine changes, including an increased production and release of catecholamines, renin, angiotensin, and vasopressin. These changes contribute to the postnatal increase in systemic vascular resistance and a decrease in systemic blood flow. If the neonate experiences a hypoxic insult, such as perinatal asphyxia, myocardial dysfunction may occur, contributing to hypotension [14]. Preterm infants often require a positive pressure ventilation to support respiration, which can reduce systemic blood flow by increasing intrathoracic pressure and decreasing venous return [15]. Sepsis, necrotizing enterocolitis, and chronic colitis are common causes of hypotension in preterm and term infants. These conditions lead to the release of inflammatory mediators, such as interleukin-1 and tumor necrosis factor, which cause peripheral vasodilation and increased vascular permeability. These result in hypovolemia and hypotension [16]. Relative adrenal insufficiency occurs when the body is unable to produce adequate cortisol in response to stress or illness, contributing to hypotension in premature infants. Preterm neonates are particularly vulnerable to this condition due to the immaturity of the adrenal glands. They have limited 3β-hydroxy steroid dehydrogenase, an enzyme necessary for cortisol synthesis. The hypothalamic-pituitary axis is suppressed by maternal cortisol transmitted through the placenta [17]. Diagnosis should be done to evaluate clinical assessment, close monitoring of infants with hypotension, echocardiography, and consider contributing causes and interventions [18]. With regard to anti-hypotensive medication used in neonates, treatment approaches typically include volume expansion, vasoactive medications, and corticosteroids. In most neonatal intensive care units, initial management often involves volume expansion using intravenous colloids or crystalloids, which is administered in 85.0% of preterm infants. This is typically followed by the use of anti-hypotensive agents. These agents include vasoactive medications (inotropes and vasopressors) and corticosteroids [19]. Vasopressor drugs affect vascular tone and are further divided into vasoconstrictors, including pure vasoconstrictors like phenylephrine and arginine vasopressin, as well as constrictors such as dopamine, epinephrine, and norepinephrine. Inotropes drugs enhance myocardial contractility to improve cardiac output such as dobutamine and milrinone [19]. This study was designed to compare the neonatal characteristics, clinical practices, treatment indications, and outcomes of neonates admitted to a public hospital and a private clinic in Libya.

Materials and methods

Study design and setting: A cross-sectional observational study was conducted over four months from December 2024 to April, at a public tertiary center and private clinic.

Study sample: A total of 120 neonates diagnosed with hypotension and treated in NICUs at both institutions were included. Inclusion criteria included neonates less than 45 days of age with a documented hypotensive episode requiring pharmacologic intervention.

Data collection: Data were collected using a pre-validated self-designed structured questionnaire, which captured neonatal demographic, gestational age and birth weight, systolic and diastolic blood pressure (BP) measurement with the method used, echocardiography findings, primary indication for treatment, choice, dosage, and administration of antihypotensive agents, duration and titration of treatment, monitored parameters, clinical response including time to BP normalization, adverse effects, and neonatal outcomes including recovery, persistent hypotension, complications, or mortality.

Ethical considerations: The study was conducted in accordance with ethical standards and was approved by the institutional review board (IRB) in both settings. Written consent from the parent of the patient was signed and was completely voluntary. All the needed information for patient or parent was presented by using local and simplified terms for a disease in their common language. Patient information was kept confidential.

Statistical analysis: All analyses were performed using SPSS version 29.1.1. Descriptive statistics, including mean, median, frequency, and percentage, were computed. Comparisons between the two settings were conducted by using the Chi-square test for categorical variables, and the Mann-Whitney *U*-test for continuous variables, as appropriate. A p-value of less than 0.05 was considered significant.

Results

Demographic and birth characteristics: Cesarean delivery (C-section) was more frequent in the private NICU (36/50; 72.0%) compared to the public NICU (45/70; 64.3%). In the private NICU, most neonates had a gestational age at birth greater than 37 weeks (37/50; 74.0%), followed by those with a gestational age of 32-36 weeks (12/50; 24.0%). In contrast, in the public NICU, the majority of neonates had a gestational age at birth of 32-36 weeks (30/70; 42.8%), followed by 28-32 weeks (23/70; 32.8%). The distribution of gestational age groups between the two sectors was highly significant (p<0.001). Neonatal age and weight were also higher in the private NICU, with a median age of 6.5 days (range: 2-17) versus one day (range: 1-1) in the public NICU, and a median weight of 2.925 Kg (2.29-3.355) compared to 2.175 Kg (1.775-2.900); these differences were highly significant (p<0.001, **Table 1**). Resuscitation at birth did not differ significantly between the two NICU settings. In contrast, congenital anomalies or neonatal infections were significantly more frequent in the public NICU, with seven neonates affected in the private NICU versus 24 in the public NICU (p<0.01) (**Table 1**).

Clinical assessment of hypotension: In the private NICU, systolic median 40 mmHg (30.0-55.0), median diastolic BP 28 mmHg (20.75-38.5) were lower compared to the public NICU, systolic median BP 73 mmHg (range: 62-88.75), median diastolic BP 38 mmHg (26.0-45.0) and these differences were highly significant (p<0.001) for both readings. In contrast, there were no significant differences regarding the method of mean BP measurement (p=0.417); the majority in both NICUs used the Oscillometric method. Meanwhile, there were highly significant difference (p<0.001) for the Echocardiographic findings in the private NICU; more than half of the neonates were normal, in contrast to the public NICU, which did not perform Echocardiography (**Table 2**).

Table 1: Demographic profile of neonates admitted to the Neonatal Intensive Care Unit

Demographic variable	Total n=120 (%) Median (IQR)	Private NICU n=50 (%) Median (IQR)	Public NICU n=70 (%) Median (IQR)	X²/U Mann-Whitney test	P
Type of delivery				0.791	0.37
Vaginal	39 (32.5%)	14 (28.0%)	25 (35.7%)		
Cesarean	81 (67.5%)	36 (72.0%)	45 (64.3%)		
Gestational age at birth				37.15	**< 0.001**
< 28 weeks	01 (0.9%)	0.0	01 (01.4%)		
28-32 weeks	24 (20.0%)	01 (2.0%)	23 (32.8%)		
32-36 weeks	42 (35.0%)	12 (24.0%)	30 (42.8%)		
≥ 37 weeks	53 (44.1%)	37 (74.0%)	16 (23.0%)		
Neonate age (days)	1.0 (1-8)	6.5 (2-17)	1.0 (1-1)	565.0	**< 0.001**
Neonate weight (Kg)	2.4 (2.4-3.1)	02.925 (2.29-3.355)	02.175 (1.775-2.9)	965	**< 0.001**
Resuscitation required				0.00	1.000
Yes	19 (15.9%)	08 (16.0%)	11 (15.7%)		
No	101 (84.1%)	42 (84.0%)	59 (84.3%)		
Congenital anomalies or infection				6.26	**< 0.01**
No	89 (74.2%)	43 (86.0%)	46 (65.7%)		
Yes	31 (25.8%)	7 (14.0%)	24 (34.3%)		

Table 2: Clinical assessment of hypotension for neonates admitted to the Neonatal Intensive Care Unit

Clinical assessment of hypotension	Total n=120 (%) Median (IQR)	Private NICU n=50 (%) Median (IQR)	Public NICU n=70 (%) Median (IQR)	X²/U Mann-Whitney test	P
Systolic BP (mmHg)	62 (43.0-80.5)	40 (30.0-55.0)	73 (62.0-88.75)	301.5	**< 0.001**
Diastolic BP (mmHg)	32.5 (24.0-43.0)	28 (20.75-38.5)	38 (26.0-45.0)	1194	**< 0.01**
Mean BP measurement method				1.76	0.417
Oscillometric	119 (99.2)	49 (98)	70 (100)		
Invasive	01 (0.8)	01 (2)	0		
Echocardiographic finding				96.73	**< 0.001**
None	55 (45.8)	05 (10)	50 (71.4)		
Normal	33 (27.5)	32 (64)	01 (1.4)		
PDA	06 (5.0)	06 (12)	0		
PFO	07 (5.8)	01 (2)	06 (8.5)		
ASD	09 (7.5)	01 (2)	08 (11.4)		
VSD	02 (1.7)	0.0	02 (2.8)		
PPHN	02 (1.7)	02 (4)	0		
PDA+PFO	02 (1.7)	02 (4)	0		
PDA+ASD	02 (1.7)	0.0	02 (2.8)		
PDA+AVSD	01 (0.8)	0.0	01 (1.4)		
PFO+PPA	01 (0.8)	01 (2)	0 (0.0)		

PDA: Patent Ductus Arteriosus, PFO: Patent Foramen Ovale, ASD: Atrial Septal Defect, VSD: Ventricular Septal Defect, PPHN: Persistent Pulmonary Hypertension of the Newborn

Indication for antihypotension treatment: There were significant differences in the indications for antihypotensive treatment between the two NICUs (p<0.001). In the private NICU, hypotension was the predominant reason for treatment (20/50; 40.0%). In contrast, in the public NICU, poor perfusion was the primary indication (32/70; 45.7%), showing a highly significant difference (p<0.001). Regarding the definition of hypotension, the public NICU relied on clinical signs (56/70; 80.0%), whereas the private NICU depended on systolic BP measurements (26/50; 56.0%). Thus, the public NICU used non-pharmacological interventions more frequently than the private NICU (66.0% vs. 20.0%, respectively) (**Table 3**).

Table 3: Indications for anti-hypotension treatment for neonates admitted to the Neonatal Intensive Care Unit

Indications for anti-hypotension Treatment	Total n=120 (%) Median (IQR)	Private NICU n=50 (%) Median (IQR)	Public NICU n=70 (%) Median (IQR)	X²/U Mann-Whitney test	P
Primary reason				33.33	**< 0.001**
Hypotension	32 (26.7)	20 (40)	12 (17.1)		
Poor perfusion	40 (33.3)	08 (16)	32 (45.7)		
Sepsis	08 (6.7)	06 (12)	02 (02.8)		
Other	01 (0.8)	01 (2)	0		
Multiple responses	39 (32.5)	15 (30)	24 (34.2)		
Hypotension defined				75.45	**< 0.001**
MAP	10 (8.3)	09 (18)	01 (1.4)		
Systolic BP	29 (24.2)	28 (56)	01 (1.4)		
Clinical Sign	65 (54.2)	09 (18)	56 (80)		
Other	04 (3.3)	02 (04)	02 (2.8)		
Multiple responses	12 (10)	02 (04)	10 (14.2)		
Non-pharmacological interventions				25.9	**< 0.001**
Yes	73 (60.8)	17 (34)	56 (80)		
No	47 (39.2)	33 (66)	14 (20)		

Drug administration: Highly significant differences in the pattern of antihypotensive drug use between the two NICUs were observed (p<0.001). In the public NICU, dopamine was the predominant agent administered (60/70; 85.7%). In contrast, the private NICU more commonly used combination therapy (21/50; 42%). Dopamine did not differ significantly between the two settings. However, dobutamine was used exclusively in the private NICU at a median dose of 5.0 µg/kg/min (0.00-6.25 µg/kg/min), and this difference was highly significant (p<0.001). There were no significant differences regarding dose titration during treatment between the units. Regarding the duration of treatment, a highly significant difference was observed (p<0.001). For treatments lasting for less than 24 hours, both NICUs showed similar proportions. However, beyond 24 hours, the private NICU showed a decline in the number of treated neonates, whereas the public NICU showed an increasing trend, particularly in treatments lasting more than 48 hours (**Table 4**).

Monitoring and outcome: For the private NICU, the majority of monitored parameters were BP (26/50; 52.0%), whereas the public NICU monitored more than one parameter (58/70; 82.8%), and this difference was very highly significant (p<0.001). Accordingly, both settings showed a significant difference in the response to treatment (p<0.001), with a faster response observed in the private NICU (Median=9 hrs. vs 24 hrs.) compared to the public NICU. Similarly, both settings showed improvement in clinical signs, which was also significant (p<0.05). In contrast, the public NICU reported more adverse effects (21/70; 30.0%) and correspondingly more deaths (23/70; 32.8%), compared to four deaths in the private NICU (p<0.001) (**Table 5**).

Table 4: Drug administration for neonates admitted to the Neonatal Intensive Care Unit

Drug administration	Total n=120 (%) Median (IQR)	Private NICU n=50 (%) Median (IQR)	Public NICU n=70 (%) Median (IQR)	X²/U Mann-Whitney test	P
Pharmacological treatment				40.46	**< 0.001**
Dopamine	76 (63.3)	16 (32.0)	60 (85.7)		
Dobutamine	08 (6.7)	08 (16.0)	0		
Epinephrine	03 (2.5)	03 (6.0)	0		
Norepinephrine	01 (0.8)	01 (2.0)	0		
Vasopressin	01 (0.8)	01 (2.0)	0		
Multiple drugs used	31 (25.8)	21 (42.0)	10 (14.2)		
Dopamine dose (mcg/kg/min)	05 (3.0-8.0)	05 (0.0-10.0)	03 (3.0-5.75)	1608	= 0.436
Dobutamine dose (mcg/kg/min)	0 (0.0-5.0)	5 (0.0-6.25)	0	1093	**< 0.001**
Another dose (mcg/kg/min)	0	0	0	1566	= 0.80
Titration during treatment				0.00	= 1.000
Yes	71 (59.2)	30 (60.0)	41 (58.5)		
No	49 (40.8)	20 (40.0)	29 (41.4)		
Duration of treatment				9.80	**< 0.01**
< 24 hr.	66 (55.0)	34 (68)	32 (45.7)		
24-48 hr.	25 (20.8)	11 (22)	14 (20.0)		
> 48 hr.	29 (24.2)	05 (10)	24 (34.2)		

Table 5: Monitoring and outcomes for neonates admitted to the Neonatal Intensive Care Unit

Monitoring and outcomes	Total n=120 (%) Median (IQR)	Private NICU n=50 (%) Median (IQR)	Public NICU n=70 (%) Median (IQR)	X²/U Mann-Whitney test	P
Parameters were monitored				41.36	**< 0.001**
BP	33 (27.5)	26 (52)	07 (10)		
Urine output	5 (4.2)	05 (10)	0		
Capillary refill time	10 (8.3)	05 (10)	05 (7.14)		
More than one	72 (60.0)	14 (28)	58 (82.8)		
Response to treatment				9.43	**< 0.01**
Yes	94 (78.3)	46 (92)	48 (68.5)		
No	26 (21.7)	04 (08)	22 (31.4)		
Time to normalization (TTN) - hrs.	16 (3.0-36.0)	09 (5.5-16.0)	24 (0.0-48.0)	1304	**< 0.01**
Improvement in clinical signs				4.83	**< 0.05**
Yes	91 (75.8)	43 (86)	48 (68.6)		
No	29 (24.2)	07 (14)	22 (31.4)		
Adverse effects observed				11.87	**< 0.001**
Yes	24 (20.0)	03 (06)	21 (30.0)		
No	96 (80.0)	47 (94)	49 (70.0)		
Outcomes				11.85	**< 0.001**
Recovery	92 (76.7)	45 (90)	47 (67.1)		
Persistent hypotension	01 (0.8)	01 (02)	0		
Death	27 (22.5)	04 (08)	23 (32.8)		

Discussion

The current study aligns with the Donabedian quality framework [20]. Highlight the substantial differences in structure, processes, and clinical outcomes in neonatal care and outcomes between public and private NICUs. It was designed to compare neonatal characteristic, clinical practice, treatment indication, and outcome between the two settings. The findings revealed a higher rate of cesarean delivery in the private NICU, concordant with global trends reporting elevated C-section rates in the private sector [21]. Significantly higher gestational ages (≥ 37 weeks) and birth weights were predominantly in neonates admitted to the private NICU, while the public NICU had a larger proportion of preterm infants (28-36 weeks). These case-mix differences are clinically relevant, as prematurity and low birth weight are well-established risk factors for neonatal morbidity and mortality [22-24]. The variations may reflect differences in referral pathways, socioeconomic factors, and disparities in access to antenatal care or institutional policies. Although these inequalities in the study showed no significant differences in resuscitation rates, congenital anomalies, and neonatal infections were more prevalent in the public NICU. This is in line with evidence that public hospitals often receive complicated or high-risk cases, and that populations served by public facilities may have limited access to prenatal screening [25, 26]. BP was predominantly assessed through Oscillometric measurements across both settings. Notably, systolic and diastolic BP were significantly lower in the private NICU despite that setting managing neonates who were generally more mature and less clinically complex. Although the public NICU had higher rates of prematurity, sepsis, and congenital anomalies-conditions typically associated with hypotension [26], the measured BP values were higher. This inconsistency likely reflects differences in measurement timing, cuff selection, device accuracy, or operational definitions of hypotension rather than true physiological divergence. Such methodological variation is well-recognized as a major source of inconsistency in neonatal hemodynamic assessment. Nearly all neonates in the private NICU underwent echocardiography assessment, an increasingly recommended tool for hemodynamic evaluation and identification of structural cardiovascular anomalies such as PDA, ASD, and PFO, which was more frequently utilized [26]. In contrast, the public NICU relied more heavily on clinical signs, increasing the likelihood of underdiagnosis of cardiac pathology. These differences extended into the criteria for initiating treatment: hypotension was the predominant indication in the private NICU, whereas poor perfusion-often detected clinically-was more common in the public NICU. Such variability is likely rooted in resource availability and diagnostic workflows. Non-pharmacologic measures were more frequently used in the public NICU before initiating medications, whereas the private NICU is more commonly proceeded directly to pharmacologic intervention. Dopamine was the primary antihypotensive agent used in the public NICU, reflecting its established role as a first-line therapy and its broad availability [27, 28]. In the private NICU, combination regimens, including dopamine plus dobutamine, were more frequently employed. Early evidence demonstrates dopamine's superior ability to rapidly increase systolic and diastolic BP compared with dobutamine, although this may occur at the expense of decreased regional perfusion due to vasoconstriction [27]. Cochrane evidence further supports dopamine as more effective in achieving immediate BP stabilization, while dobutamine provides more pronounced improvements in cardiac output, making it preferable when myocardial dysfunction is suspected [28].

A recent systematic review shows that although dopamine remains the most widely used first-line agent, private and better-resourced centers increasingly adopt combination therapies guided by echocardiographic parameters [29]. This evolution parallels international trends showing greater therapeutic diversification in high-resource units [30]. The private NICU achieved BP stabilization more frequently within 24 hours, whereas the public NICU had more cases requiring therapy beyond 48 hours. This likely reflects the more complex neonatal profile in the public setting and the reliance on single-agent dopamine therapy. Evidence shows that dopamine effectively

restores BP in the short term, but more severe or refractory cases may require additional inotropes, which were more accessible in the private NICU [28, 30]. And this may have contributed to the faster stabilization observed. Regarding monitoring and outcomes, the private NICU employed more focused monitoring, primarily BP, while the public NICU monitored multiple parameters simultaneously, likely due to differing clinical protocols and staffing ratios. Overall, the private NICU demonstrated faster clinical improvement, shorter median time to normalization of BP (9 hrs. vs. 24 hrs.), fewer adverse effects, and lower mortality. Conversely, the public NICU experienced delayed responses and higher complication rates, consistent with resource constraints and the more complex case mix. These findings parallel those of Dwivedi and others [31] who similarly reported significantly higher survival rates in private NICUs compared with public facilities in India. The observational design precludes causal inference, differences in baseline neonatal characteristics between institutions introduce case-mix bias, and the modest sample size limits generalizability.

Conclusion: This study highlights significant differences in neonatal characteristic, clinical practice, treatment indication, and outcomes between the public and private NICUs. Neonates in the private NICU were more mature, had higher birth weights, and received more targeted pharmacological interventions guided by Echocardiography, leading to faster blood pressure stabilization, reduced adverse effects, and lower mortality. Conversely, a higher proportion of preterm neonates in the public NICU relied more on clinical assessment and non-pharmacological interventions, experiencing slower responses to treatment and higher mortality rates.

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