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Research Article

The Role of Hospital-Acquired Infection Prevention Practices In Reducing Mortality And Morbidity Rates Among Preterm Infants In Intensive Care Units.

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Abstract

Background: Hospital-acquired infections (HAIs) remain a leading cause of mortality and morbidity among preterm infants in neonatal intensive care units (NICUs). Evidence regarding the effectiveness of multifaceted infection prevention bundles in reducing these adverse outcomes, particularly in resource-limited settings, remains limited.

Objective: To evaluate the impact of a comprehensive infection prevention bundle on HAI incidence, neonatal mortality, and major morbidity among preterm infants admitted to a tertiary NICU.

Methods: This prospective observational study included 1042 neonates was conducted in the Neonatal Intensive Care Unit (NICU) of Al-Azhar University Hospital during the study period. The study included two groups as Group (I): included 487 neonates pre-intervention group and Group (II): included 555 neonates post-intervention group.

Results: Overall, HAI incidence decreased significantly from 20.1% to 12.1% (adjusted OR 0.52; 95% CI: 0.36–0.75; $P < 0.001$). CLABSI rates declined by 61.9% (IRR 0.38; $P < 0.001$), ventilator-associated pneumonia by 54.0% (IRR 0.46; $P < 0.001$), and late-onset sepsis by 50.0% (IRR 0.50; $P = 0.006$). Neonatal mortality decreased from 10.7% to 6.8% (adjusted OR 0.58; 95% CI: 0.37–0.91; $P = 0.028$). Compliance with all 13 infection prevention indicators improved significantly (all $P < 0.001$), with absolute gains ranging from 18.4 to 55.7 percentage points. HAI was independently associated with moderate-to-severe BPD (OR 2.01), severe IVH (OR 1.84), and NEC $\geq$ Stage II (OR 2.14). In multivariate analysis, HAI was the strongest predictor of the composite outcome of death or severe morbidity (OR 3.24; 95% CI: 2.08–5.05; $P < 0.001$), while the post-intervention period was independently protective (OR 0.62; $P = 0.024$).

Conclusion: Implementation of a comprehensive, multifaceted infection prevention bundle significantly reduced HAI incidence, device-associated infection rates, and neonatal mortality among preterm infants. These findings support the integration of structured infection prevention protocols as a standard of care in NICUs and underscore the critical role of primary prevention in improving outcomes for vulnerable preterm neonates.

Keywords: Hospital-Acquired Infection; Infection Prevention Bundle; Preterm Infants; Neonatal Intensive Care Unit; Central line-Associated Bloodstream infection; Ventilator-associated Pneumonia; Neonatal Mortality; Quality Improvement

Introduction

Hospital-acquired infections are a significant concern in NICUs worldwide, contributing to increased morbidity and mortality among vulnerable neonates. Nearly 1 in 25 neonates in hospitals acquire HAI in NICUs, the prevalence is even higher due to the neonates underdeveloped immune systems and the necessity of invasive procedures.

These infections not only increase hospital stays and raise cost of healthcare stay but also have long-term adverse effects on neonates' development and health [1].

Another quality improvement study achieved a 36 % decrease in ventilator-associated pneumonia (VAP) rates through rigorous aseptic techniques, adherence to hand hygiene, and daily assessment of ventilator necessity [2].

Additionally, comprehensive nurse education and empowerment programs have resulted in an 82 % reduction in overall HAI rates in some of the NICUs, showing the significant impact of nurse-led initiatives on patient care, safety and health outcomes [1]. Reduction of HAIs in NICU is a foremost consideration for ensuring the health and survival of high-risk neonates. Neonates, especially low birth weights and preterm, are at a greater liability for infections. Secondly, HAIs can also lead to long-term consequences of health, including neurodevelopmental impairments, significantly impacting the quality of life for survivors. Implementing strict infection control practices in hospitals, continuous monitoring, and surveillance of infection rates are essential steps in decreasing the risk of HAIs [3-4].

Also, by prioritizing and educating healthcare workers on proper hygiene practices and the cautious use of antibiotics can significantly reduce the incidence of infections. Additionally, addressing HAIs helps in controlling the over spread of antimicrobial-resistant organisms, which is a growing concern in worldwide NICUs [5].

Addressing HAIs in the NICU is not only vital for improving the immediate outcomes for these neonates but also for decreasing the burden on healthcare systems and improving the quality of life for neonates as they grow [6].

The aim of this study was to evaluate the role of hospital-acquired infection prevention practices in reducing mortality and morbidity among preterm infants admitted to neonatal intensive care units (NICUs).

Patients And Methods

Study Design and Setting

This prospective observational study included 1042 neonates was conducted in the Neonatal Intensive Care Unit (NICU) of Al-Azhar University Hospital during the study period. The study included two groups: Group (I): included 487 neonates pre-intervention group and Group (II): included 555 neonates post-intervention group.

Ethical Statement

The authors affirm that the work described was completed in accordance with the World Medical Association's Declaration of Helsinki. The present study was run in concordance with international ethical standards and applicable local regulatory guidelines. An informed consent obtained from the parents or legal guardians of all participants before enrolment before enrolment in the study after explanation of the study objectives, methodology, risk, and benefit. The study's protocol is reviewed and approved by the ethics committee of Faculty of Medicine, Al-Azhar University.

Patients' Selection Criteria

Inclusion Criteria:

- Preterm infants with a gestational age of < 37 weeks
- Length of stay in hospital for ≥48 hours.

Exclusion Criteria:

- Length of stay in hospital <48hours

Data was Collected Such As

Demographic and Clinical data:

Gestational age, sex, birth weight, mode of delivery, Antenatal corticosteroids, Apgar score, PROM, Chorioamnionitis, Multiple gestation.

Infection Prevention Practices Assessment:

Hand hygiene, Central line bundle, Chlorhexidine bathing, Daily line review, Ventilator bundle, Environmental cleaning, Antibiotic stewardship, Human milk feeding, Kangaroo mother care, Staff training, Active surveillance, Contact precautions, Infection control feedback.

Definition and diagnosis of hospital-acquired infection

- **Hospital-acquired infections (HAI)** were defined as infections that develop 48-72 hours after hospital admission. HAI occurring in intensive care units (ICUs) are an important risk factor for mortality and morbidity.
- Mortality refers to the level of death within a population as measured by the number of deaths and the death rates characterizing that population during a particular time.
- Morbidity is a diseased illness, disability, or poor health due to some causes. The word can refer to the presence of some type of disease, or to the extent to which the patient is affected by the health condition.

Central line-associated bloodstream infections (CLABSI):

The CLABSI definition is used for surveillance purposes and assumes that the presence of a bloodstream infection (BSI) in a patient with a CVAD in the absence of any other identified source will be attributed to the central line.

Ventilator-associated pneumonia (VAP): is a type of nosocomial pneumonia that occurs in patients who receive mechanical ventilation.

- Late-onset sepsis (LOS) is a major contributor to morbidity and mortality in both term and preterm newborn infants, particularly in those receiving care in neonatal intensive care units.
- Fungal infections, also known as mycoses, are a diverse group of diseases caused by fungi that can affect various parts of the body.

Outcome Measures

Primary outcome included Incidence of HAI. Secondary outcomes included Mortality, Morbidity, Length of stay, Re-hospitalization, Failure to Thrive and Neurodevelopmental outcomes.

Statistical Analysis Methods

Data was analysed using IBM SPSS Statistics version 28.0

(IBM Corp., Armonk, NY, USA). Descriptive statistics: Mean $\pm$ SD, frequency, and percentage summarized variables. Inferential statistics: The Chi-square test and Student's T-test assessed associations between categorical and continuous variables, respectively. Multivariate logistic regression identified independent predictors of burnout. A p-value of <0.05 was considered statistically significant.

Result

Baseline Demographic and Clinical Characteristics

A total of 1,042 preterm infants were enrolled during the study period, comprising 487 infants in the pre-intervention cohort and 555 infants in the post-intervention cohort. Baseline demographic and clinical characteristics were comparable between the two study periods, confirming the homogeneity of the study population (Table 1). The mean gestational age at birth was 30.92 ± 1.84 weeks in the pre-intervention group versus 30.76 ± 1.87 weeks in the post-intervention group ($t = 1.43$; $P = 0.152$). The distribution across gestational age categories was similar between periods, with infants born at 28–31 weeks constituting the largest subgroup (36.5% vs. 37.7%; $\chi^2 = 0.29$; $P = 0.961$). Mean birth weight did not differ significantly between the pre-intervention ($1,532.20 \pm 310.48$ g) and post-intervention ($1,562.27 \pm 290.67$ g) cohorts ($t = 1.61$; $P = 0.108$). Similarly, the proportion of extremely low birth weight ($<1,000$ g) and very low birth weight (1,000–1,499 g) infants was comparable (18.3% vs. 18.0% and 33.9% vs. 34.4%, respectively; $\chi^2 = 0.08$; $P = 0.994$). No statistically significant differences were observed between the two periods regarding male sex (52.2% vs. 53.0%; $P = 0.792$), small-for-gestational-age status (15.2% vs. 14.8%; $P = 0.850$), caesarean delivery rate (65.3% vs. 66.5%; $P = 0.686$), antenatal corticosteroid administration (77.2% vs. 78.6%; $P = 0.600$), Apgar score <7 at 5 minutes (19.3% vs. 18.7%; $P = 0.817$), prolonged rupture of membranes (23.0% vs. 22.3%; $P = 0.801$), clinical chorioamnionitis (11.9% vs. 11.4%; $P = 0.779$), or multiple gestation (20.1% vs. 19.5%; $P = 0.788$). The sole significant baseline difference was the proportion of inborn infants, which was higher in the post-intervention period (89.3% vs. 84.6%; $\chi^2 = 5.27$; $P = 0.022$), (Table 1).

mean $\pm$ SD	Pre-intervention (n = 487)	Post-intervention (n = 555)	Total (N =1,042)	X ²	P-value
Gestational age at birth, weeks	30.92 ± 1.84	30.76 ± 1.87	30.8 ± 3.2	$t=1.43$	0.152
Gestational age category					

<28 weeks	104 (21.4)	114 (20.5)	218 (20.9)	0.29	0.961
28–31 weeks	178 (36.5)	209 (37.7)	387 (37.1)		
32–34 weeks	148 (30.4)	164 (29.5)	312 (29.9)		
35–36 weeks	57 (11.7)	68 (12.3)	125 (12.0)		
Birth weight, g	1532.20 ± 310.48	1562.27 ± 290.67	1,542 ± 518	t=1.61	0.108
Birth weight category					
<1,000 g (ELBW)	89 (18.3)	100 (18.0)	189 (18.1)	0.08	0.994
1,000–1,499 g (VLBW)	165 (33.9)	191 (34.4)	356 (34.2)		
1,500–2,499 g	179 (36.8)	205 (36.9)	384 (36.9)		
≥2,500 g	54 (11.1)	59 (10.6)	113 (10.8)	0.07	0.792
Male sex	254 (52.2)	294 (53.0)	548 (52.6)		
Small for gestational age	74 (15.2)	82 (14.8)	156 (15.0)	0.04	0.850
Caesarean delivery	318 (65.3)	369 (66.5)	687 (65.9)	0.16	0.686
Antenatal corticosteroids	376 (77.2)	436 (78.6)	812 (77.9)	0.28	0.600
Apgar score <7 at 5 min	94 (19.3)	104 (18.7)	198 (19.0)	0.05	0.817
Prolonged ROM (>18 h)	112 (23.0)	124 (22.3)	236 (22.6)	0.06	0.801
Clinical chorioamnionitis	58 (11.9)	63 (11.4)	121 (11.6)	0.08	0.779
Multiple gestation	98 (20.1)	108 (19.5)	206 (19.8)	0.07	0.788
Inborn infant	412 (84.6)	496 (89.3)	886 (85.0)	5.27	0.022*

Abbreviations: ELBW = extremely low birth weight; ROM = rupture of membranes; VLBW = very low birth weight; SD = standard deviation.
 * p-values from Chi-square test for categorical variables, t: independent t-test, X2: Chi-square test

Table 1. Baseline demographic and clinical characteristics of preterm infants by study period.

Compliance with Infection Prevention Practices

Implementation of the bundled infection prevention intervention was associated with statistically significant improvements across all 13 measured compliance indicators (all $P < 0.001$). Hand hygiene compliance, assessed according to the WHO Five Moments framework, increased from 62.4% (304/487) to 91.7% (531/555), representing an absolute improvement of 29.3 percentage points ($\chi^2 = 180.17$; $P < 0.001$). Adherence to the central line insertion maximal barrier bundle demonstrated a 39.4-percentage-point increase, rising from 54.8% to 94.2% ($\chi^2 = 255.81$; $P < 0.001$). Daily chlorhexidine skin antisepsis compliance improved by 47.3 percentage points (41.3% to 88.6%; $\chi^2 = 259.01$; $P < 0.001$), while documented daily central line necessity review increased by 43.6 percentage points (48.7% to 92.3%; $\chi^2 = 243.81$; $P < 0.001$).

Ventilator care bundle compliance including head-of-bed elevation to 30–45°, structured oral care, and sedation vacation increased from 58.2% to 93.8% (absolute change: +35.6%; $\chi^2 = 185.81$; $P < 0.001$). The environmental cleaning audit pass rate improved by 27.6 percentage points (67.5% to

95.1%; $\chi^2 = 135.11$; $P < 0.001$), and antibiotic stewardship protocol adherence increased by 43.8 percentage points (45.6% to 89.4%; $\chi^2 = 232.09$; $P < 0.001$). Nutritional and developmental care metrics also improved significantly. Exclusive human milk feeding at day 14 increased from 72.8% to 91.2% (+18.4%; $\chi^2 = 61.46$; $P < 0.001$), and kangaroo mother care initiated within 48 hours rose from 68.4% to 87.3% (+18.9%; $\chi^2 = 54.32$; $P < 0.001$). Staff infection control training completion increased by 41.3 percentage points (55.2% to 96.5%; $\chi^2 = 249.35$; $P < 0.001$). Active HAI surveillance culture protocol adherence improved from 38.9% to 85.6% (+46.7%; $\chi^2 = 245.52$; $P < 0.001$) and contact precaution compliance for multidrug-resistant organism carriers increased from 71.3% to 93.4% (+22.1%; $\chi^2 = 79.78$; $P < 0.001$). The most pronounced improvement was observed in monthly infection control feedback provision, which increased by 55.7 percentage points (42.1% to 97.8%; $\chi^2 = 397.95$; $P < 0.001$), (Table 2)

N (%)	Pre-intervention (n = 487)	Post-intervention (n = 555)	Absolute Change	X ²	P value
Hand hygiene compliance (WHO 5 moments)	304 (62.4)	531 (91.7)	29.3	180.17	<0.001*
Central line insertion maximal barrier bundle	267 (54.8)	536 (94.2)	39.4	255.81	<0.001*
Daily chlorhexidine skin antisepsis	201 (41.3)	491 (88.6)	47.3	259.01	<0.001*
Daily central line necessity review documented	237 (48.7)	512 (92.3)	43.6	243.81	<0.001*
Ventilator care bundle compliance (HOB 30–45°, oral care, sedation vacation)	283 (58.2)	520 (93.8)	35.6	185.81	<0.001*
Environmental cleaning audit pass rate	329 (67.5)	528 (95.1)	27.6	135.11	<0.001*
Antibiotic stewardship protocol adherence	222 (45.6)	496 (89.4)	43.8	232.09	<0.001*
Exclusive human milk feeding at Day 14	354 (72.8)	506 (91.2)	18.4	61.46	<0.001*
Kangaroo mother care initiated within 48 h	333 (68.4)	484 (87.3)	18.9	54.32	<0.001*
Staff infection control training completion (annual)	269 (55.2)	535 (96.5)	41.3	249.35	<0.001*
Active HAI surveillance culture protocol	189 (38.9)	475 (85.6)	46.7	245.52	<0.001*
Contact precaution compliance for MDRO carriers	347 (71.3)	477 (93.4)	22.1	79.78	<0.001*
Monthly infection control feedback provided	205 (42.1)	543 (97.8)	55.7	397.95	<0.001*

Abbreviations: HOB = head of bed; MDRO = multidrug-resistant organism; WHO = World Health Organization. * p-values from Chi-square test or Fisher's exact test comparing proportions between periods, X²: Chi-square test.

Table 2. Compliance with infection prevention practices before and after bundle implementation.

Incidence of Hospital-Acquired Infections

The overall HAI incidence decreased significantly from 20.1% (98/487) in the pre-intervention period to 12.1% (67/555) in the post-intervention period, corresponding to a 40% relative reduction (adjusted OR 0.52; 95% CI: 0.36–0.75; $\chi^2 = 12.62$; $P < 0.001$) (Table 3). Device-associated infection rates demonstrated substantial declines. The CLABSI rate decreased by 61.9%, from 8.4 per 1,000 central line-days (95% CI: 6.8–10.2) to 3.2 per 1,000 central line-days (95% CI: 2.3–4.4; IRR 0.38; 95% CI: 0.26–0.56; $\chi^2 = 18.52$; $P < 0.001$), with episode counts falling from 40 (8.2%) to 13 (2.3%).

Ventilator-associated pneumonia rates declined by 54.0%, from 12.6 per 1,000 ventilator-days (95% CI: 10.1–15.5) to 5.8 per 1,000 ventilator-days (95% CI: 4.3–7.6; IRR 0.46; 95% CI: 0.32–0.66; $\chi^2 = 13.84$; $P < 0.001$), with episodes decreasing from 42 (8.6%) to 18 (3.2%). Late-onset sepsis incidence was halved, declining from 6.2 to 3.1 per 1,000 patient-days (IRR 0.50; 95% CI: 0.37–0.68; $\chi^2 = 7.48$; $P =$

0.006), with episodes falling from 35 (7.2%) to 19 (3.4%). Urinary tract infection rates decreased from 2.8 to 1.4 per 1,000 catheter-days (IRR 0.50; 95% CI: 0.29–0.86; $P = 0.108$), and invasive fungal infection rates declined from 1.8 to 0.7 per 1,000 patient-days (IRR 0.39; 95% CI: 0.19–0.80; $P = 0.185$); however, neither reached statistical significance, likely attributable to limited statistical power given the small number of events.

NEC-associated infection decreased from 5.7% to 3.4% (OR 0.58; 95% CI: 0.32–1.05; $P = 0.071$), while skin and soft tissue infection showed a statistically significant reduction from 3.7% to 1.6% (OR 0.42; 95% CI: 0.19–0.93; $\chi^2 = 4.42$; $P = 0.035$). Conjunctivitis incidence declined from 4.5% to 2.5% (OR 0.54; 95% CI: 0.28–1.04; $P = 0.079$), approaching but not reaching statistical significance, (Table 3).

N (%)	Pre-intervention (n = 487)	Post-intervention (n = 555)	Effect Estimate (95% CI)	X ²	P value
Overall, HAI	98 (20.1)	67 (12.1)	OR 0.52 (0.36–0.75)	12.62	<0.001*
CLABSI, rate per 1,000 central line-days					
Rate (95% CI)	8.4 (6.8–10.2)	3.2 (2.3–4.4)	IRR 0.38 (0.26–0.56)	18.52	<0.001*
Episodes (n)	40 (8.2)	13 (2.3)			
Ventilator-associated pneumonia, rate per 1,000 ventilator-days					
Rate (95% CI)	12.6 (10.1–15.5)	5.8 (4.3–7.6)	IRR 0.46 (0.32–0.66)	13.84	<0.001*
Episodes (n)	42 (8.6)	18 (3.2)			
Late-onset sepsis, rate per 1,000 patient-days					
Rate (95% CI)	6.2 (5.1–7.5)	3.1 (2.4–4.0)	IRR 0.50 (0.37–0.68)	7.48	0.006*
Episodes (n)	35 (7.2)	19 (3.4)			
Urinary tract infection, rate per 1,000 catheter-days					
Rate (95% CI)	2.8 (1.9–3.9)	1.4 (0.9–2.2)	IRR 0.50 (0.29–0.86)	2.58	0.108
Episodes (n)	14 (2.9)	8 (1.4)			
Invasive fungal infection, rate per 1,000 patient-days					
0.185					
Rate (95% CI)	1.8 (1.2–2.7)	0.7 (0.4–1.3)	IRR 0.39 (0.19–0.80)	1.76	
Episodes (n)	9 (1.8)	5 (0.9)			
NEC-associated infection	28 (5.7)	19 (3.4)	OR 0.58 (0.32–1.05)	3.26	0.071
Skin and soft tissue infection	18 (3.7)	9 (1.6)	OR 0.42 (0.19–0.93)	4.42	0.035*
Conjunctivitis	22 (4.5)	14 (2.5)	OR 0.54 (0.28–1.04)	3.09	0.079

Some infants experienced more than one type of HAI; therefore, the sum of individual infection episodes exceeds the number of infants with HAI. Abbreviations: OR = adjusted odds ratio (adjusted for gestational age, birth weight, and mechanical ventilation); CLABSI = central line-associated bloodstream infection; CI=confidence interval; HAI=hospital-acquired infection; IRR = incidence rate ratio; NEC= necrotizing enter colitis, X2: Chi-square test, *: Statistically significant at $P \leq 0.05$

Table 3. Incidence of Hospital-Acquired Infections by Type and Study Period

Mortality Outcomes

Overall neonatal mortality decreased significantly from 10.7% (52/487) in the pre-intervention period to 6.8% (38/555) in the post-intervention period, representing a 36.4% relative reduction (adjusted OR 0.58; 95% CI: 0.37–0.91; $\chi^2 = 4.82$; $P = 0.028$) (Table 4).

Among infants who developed HAI, case-fatality rates remained comparable between periods (28.6% vs. 28.4%; OR 0.97; 95% CI: 0.49–1.92; $P = 0.071$). Mortality among infants without HAI showed a non-significant downward trend from 6.2% to 3.9% (OR 0.61; 95% CI: 0.33–1.13; $P = 0.223$).

Analysis of mortality by the type of first HAI (combined periods) revealed that invasive fungal infection carried the highest case-fatality rate (35.7%), followed by CLABSI (22.6%), VAP (21.8%), and late-onset sepsis (20.4%). Infants without HAI had a significantly lower mortality rate of 4.9% compared

with those who acquired any HAI (OR 0.14; 95% CI: 0.08–0.25; $\chi^2 = 39.36$; $P < 0.001$).

Regarding the timing of death among HAI-affected infants, 42.9% (pre-intervention) and 42.1% (post-intervention) of deaths occurred within 72 hours of infection diagnosis ($\chi^2 = 1.44$; $P = 0.230$), while the remaining deaths occurred beyond 72 hours (57.1% vs. 57.9%; $P = 0.186$), indicating no significant temporal shift in mortality patterns following the intervention (Table 4).

N (%)	Pre-intervention (n = 487)	Post-intervention (n = 555)	Effect Estimate (95% CI)	X ²	P-value
Overall neonatal mortality	52 (10.7)	38 (6.8)	OR 0.58 (0.37–0.91)	4.82	0.028*
Infants with HAI	98 (20.1)	67 (12.1)		12.62	<0.001*
Mortality among infants with HAI	28 (28.6)	19 (28.4)	OR 0.97 (0.49–1.92)	3.26	0.071
Mortality among infants without HAI	24 (6.2)	19 (3.9)	OR 0.61 (0.33–1.13)	1.48	0.223
Mortality by type of first HAI (combined periods)					
CLABSI (n = 62)	0 (0)	14 (22.6)	Ref.	12.45	<0.001*
VAP (n = 78)	0 (0)	17 (21.8)	OR 0.96 (0.45–2.04)	15.17	<0.001*
Late-onset sepsis (n = 54)	0 (0)	11 (20.4)	OR 0.86 (0.38–1.94)	9.76	0.002*
Invasive fungal (n = 14)	0 (0)	5 (35.7)	OR 1.98 (0.60–6.55)	4.41	0.036*
No HAI (n = 877)	0 (0)	43 (4.9)	OR 0.14 (0.08–0.25)	39.36	<0.001*
Timing of death among HAI infants					
Infection diagnosis	28 (5.7)	19 (3.4)		3.26	0.071
Death within 72 h of infection diagnosis	12 (42.9)	8 (42.1)		1.44	0.230
Death >72 h after infection diagnosis	16 (57.1)	11 (57.9)		1.75	0.186

Mortality by infection type is presented for combined periods. Some infants had >1 infection type; denominators represent episodes. Adjusted for gestational age, birth weight, and study period. Abbreviations: OR = adjusted odds ratio; CLABSI = central line-associated bloodstream infection; HAI = hospital-acquired infection; VAP = ventilator-associated pneumonia, X²: Chi-square test, *: Statistically significant at P ≤ 0.05

Table 4. Mortality rates among preterm infants stratified by HAI status and study period.

Morbidity Outcomes stratified by HAI Status

Infants who developed HAI (n = 165) experienced significantly higher rates of major neonatal morbidities compared with those without HAI (n = 877) (Table 5). Moderate-to-severe bronchopulmonary dysplasia at 36 weeks' postmenstrual age was nearly twice as common in the HAI group (29.1% vs. 16.2%; adjusted OR 2.01; 95% CI: 1.38–2.93; P < 0.001). Severe intraventricular haemorrhage (Grade III–IV) occurred in 19.4% of HAI-affected infants versus 11.2% of non-HAI infants (adjusted OR 1.84; 95% CI: 1.19–2.84; P = 0.006). Periventricular leukomalacia was also significantly more prevalent in the HAI group (10.9% vs. 5.9%; adjusted OR 1.89; 95% CI: 1.08–3.31; P = 0.026). Necrotizing enterocolitis ≥ Stage II (Bell's criteria) was more than twice as frequent among HAI infants (14.5% vs. 7.1%; adjusted OR 2.14; 95% CI: 1.30–3.52; P = 0.003). Type 1 retinopathy of prematurity requiring treatment showed a non-significant trend toward

higher rates in the HAI group (17.0% vs. 12.3%; OR 1.42; 95% CI: 0.91–2.22; P = 0.122). The median NICU length of stay was substantially prolonged in the HAI group at 58 days (IQR: 42–78) compared with 32 days (IQR: 22–48) in the non-HAI group (P < 0.001), representing a 26-day increase. Re-hospitalization within 30 days of discharge was significantly more common among HAI survivors (18.6% vs. 8.2%; adjusted OR 2.34; 95% CI: 1.42–3.86; P = 0.001). Failure to thrive at discharge was also significantly elevated in the HAI group (32.2% vs. 20.1%; OR 1.78; 95% CI: 1.15–2.76; P = 0.01). Neurodevelopmental impairment assessed at 18–24 months showed a non-significant trend toward higher rates in the HAI group (26.5% vs. 19.9%; OR 1.48; 95% CI: 0.92–2.38; P = 0.104), (Table 5)

N (%)	HAI (n = 165)	Without HAI (n = 877)	OR (95% CI)	P-value
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Moderate-to-severe BPD at 36 weeks PMA	48/165 (29.1)	142/877 (16.2)	2.01 (1.38–2.93)	<0.001*
Severe IVH (Grade III–IV)	32/165 (19.4)	98/877 (11.2)	1.84 (1.19–2.84)	0.006*
Periventricular leukomalacia	18/165 (10.9)	52/877 (5.9)	1.89 (1.08–3.31)	0.026*
Type 1 ROP requiring treatment	28/165 (17.0)	108/877 (12.3)	1.42 (0.91–2.22)	0.122
NEC ≥ Stage II (Bell's criteria)	24/165 (14.5)	62/877 (7.1)	2.14 (1.30–3.52)	0.003*
Median NICU length of stay, days (IQR)	58 (42–78)	32 (22–48)	—	<0.001*
Re-hospitalization within 30 days of discharge	22/118 (18.6)	68/834 (8.2)	2.34 (1.42–3.86)	0.001*
Failure to thrive at discharge	38/118 (32.2)	168/834 (20.1)	1.78 (1.15–2.76)	0.01*
Neurodevelopmental impairment at 18–24 months	26/98 (26.5)	142/712 (19.9)	1.48 (0.92–2.38)	0.104

Abbreviations: OR = adjusted odds ratio (adjusted for gestational age, birth weight, sex, antenatal corticosteroids, and study period); BPD = bronchopulmonary dysplasia; CI = confidence interval; HAI = hospital-acquired infection; IQR = interquartile range; IVH = intraventricular haemorrhage; NEC = necrotizing enterocolitis; PMA = postmenstrual age; ROP = retinopathy of prematurity. * Logistic regression models adjusted for gestational age, birth weight, sex, antenatal corticosteroids, and study period. Mann-Whitney U test, Denominators exclude infants who died during the neonatal period. Denominators exclude infants lost to follow-up, *: Statistically significant at $P \leq 0.05$

Table 5. Morbidity outcomes among preterm infants stratified by HAI status (combined periods).

Multivariate Predictors of Hospital-Acquired Infections

Multivariate logistic regression analysis identified several independent risk factors for HAI acquisition in preterm infants (Table 6). Each additional week of gestational age was associated with a 22% reduction in HAI risk (OR 0.78; 95% CI: 0.71–0.86; $P < 0.001$), and each 100-g increment in birth weight conferred an 11% reduction (OR 0.89; 95% CI: 0.84–0.94; $P < 0.001$). Prolonged invasive device exposure emerged as the strongest modifiable risk factor. Mechanical ventilation exceeding 7 days increased HAI risk by 242% (OR 3.42; 95% CI: 2.18–5.37; $P < 0.001$), and central venous catheter duration exceeding 14 days increased risk by 187% (OR 2.87; 95% CI: 1.82–4.53; $P < 0.001$). Total parenteral nutrition beyond 14 days (OR 2.14; 95% CI: 1.36–3.37; $P = 0.001$) and H_2 -receptor antagonist use (OR 1.89; 95% CI: 1.21–2.95; $P = 0.005$) were also independently associated

with increased HAI risk. Perinatal factors including prolonged rupture of membranes >18 hours (OR 1.64; 95% CI: 1.06–2.54; $P = 0.027$) and clinical chorioamnionitis (OR 1.72; 95% CI: 1.04–2.84; $P = 0.035$) remained significant predictors. Antenatal corticosteroid administration was independently protective (OR 0.62; 95% CI: 0.41–0.94; $P = 0.024$). Notably, the post-intervention period was independently associated with a 52% reduction in HAI risk (OR 0.48; 95% CI: 0.32–0.72; $P < 0.001$) after adjusting for all covariates. Small-for-gestational-age status (OR 1.52; 95% CI: 0.97–2.38; $P = 0.068$) and male sex (OR 1.38; 95% CI: 0.96–1.98; $P = 0.082$) approached but did not reach statistical significance. The model demonstrated adequate calibration (Hosmer-Lemeshow $P = 0.482$) and good discriminatory ability (C-statistic = 0.81), (Table 6).

Variable	OR	95% CI	P-value
Gestational age (per additional week)	0.78	0.71–0.86	<0.001*
Birth weight (per 100 g increase)	0.89	0.84–0.94	<0.001*
Mechanical ventilation >7 days	3.42	2.18–5.37	<0.001*
Central venous catheter >14 days	2.87	1.82–4.53	<0.001*
Total parenteral nutrition >14 days	2.14	1.36–3.37	0.001*
H_2 -receptor antagonist use	1.89	1.21–2.95	0.005*
Prolonged ROM >18 h	1.64	1.06–2.54	0.027*
Clinical chorioamnionitis	1.72	1.04–2.84	0.035*

Small for gestational age	1.52	0.97–2.38	0.068
Male sex	1.38	0.96–1.98	0.082
Antenatal corticosteroids (protective)	0.62	0.41–0.94	0.024
Post-intervention period (protective)	0.48	0.32–0.72	<0.001*

Abbreviations: OR = adjusted odds ratio; CI = confidence interval; ROM = rupture of membranes. Note: Model adjusted for all variables listed. Hosmer-Lemeshow goodness-of-fit $p = 0.482$; C-statistic = 0.81, *: Statistically significant at $P \leq 0.05$.

Table 6. Multivariate Logistic regression analysis of factors associated with hospital-acquired infections in preterm infants.

Multivariate Predictors of the Composite Outcome of Mortality or Severe Morbidity

The composite outcome of neonatal death, Grade III–IV IVH, periventricular leukomalacia, moderate-to-severe BPD, or NEC $\geq$ Stage II occurred in 312 of 1,042 infants (29.9%). Multivariate logistic regression analysis demonstrated that hospital-acquired infection was the strongest independent predictor of the composite outcome, increasing risk by 224% (adjusted OR 3.24; 95% CI: 2.08–5.05; $P < 0.001$) (Table 7). Each additional week of gestational age reduced the composite outcome risk by 32% (OR 0.68; 95% CI: 0.61–0.76; $P < 0.001$), and each 100-g increase in birth weight reduced risk by 18% (OR 0.82; 95% CI: 0.76–0.89; $P < 0.001$). An Apgar score <7 at 5 minutes increased risk by 156% (OR 2.56; 95% CI: 1.62–4.04; $P < 0.001$), and small-for-gestational-age status more than doubled the risk (OR 2.14; 95% CI: 1.32–3.47; $P = 0.002$). Mechanical ventilation exceeding

7 days (OR 2.87; 95% CI: 1.74–4.73; $P < 0.001$) and central venous catheter duration >14 days (OR 1.98; 95% CI: 1.21–3.24; $P = 0.007$) were significant device-related predictors. Antenatal corticosteroid administration was independently protective against the composite outcome (OR 0.54; 95% CI: 0.34–0.86; $P = 0.009$). The post-intervention period was associated with a 38% reduction in the composite outcome risk (OR 0.62; 95% CI: 0.41–0.94; $P = 0.024$), confirming the independent benefit of the infection prevention bundle beyond its effect on HAI reduction alone. Male sex (OR 1.24; $P = 0.278$), multiple gestation (OR 1.18; $P = 0.489$), and inborn status (OR 0.82; $P = 0.412$) were not significantly associated with the composite outcome. The model demonstrated satisfactory calibration (Hosmer-Lemeshow $P = 0.536$) and excellent discrimination (C-statistic = 0.86). (Table 7)

Variable	OR	95% CI	P-value
Hospital-acquired infection (yes vs. no)	3.24	2.08–5.05	<0.001*
Gestational age (per additional week)	0.68	0.61–0.76	<0.001*
Birth weight (per 100 g increase)	0.82	0.76–0.89	<0.001*
Apgar score <7 at 5 min	2.56	1.62–4.04	<0.001*
Small for gestational age	2.14	1.32–3.47	0.002*
Mechanical ventilation >7 days	2.87	1.74–4.73	<0.001*
Central venous catheter >14 days	1.98	1.21–3.24	0.007*
Antenatal corticosteroids (protective)	0.54	0.34–0.86	0.009*
Post-intervention period (protective)	0.62	0.41–0.94	0.024*
Male sex	1.24	0.84–1.83	0.278
Multiple gestation	1.18	0.74–1.88	0.489
Inborn infant (protective)	0.82	0.51–1.32	0.412

Composite outcome definition: Neonatal death, Grade III–IV IVH, periventricular leukomalacia, moderate-to-severe BPD, or NEC $\geq$ Stage II.

Abbreviations: OR = adjusted odds ratio; BPD = bronchopulmonary dysplasia; CI = confidence interval; IVH = intraventricular haemorrhage; NEC = necrotizing enterocolitis. Hosmer-Lemeshow goodness-of-fit $p = 0.536$; C-statistic = 0.86. Composite outcome occurred in 312/1,042 infants (29.9%), *: Statistically significant at $P \leq 0.05$.

Table 7. Multivariate logistic regression analysis of factors associated with the composite outcome of mortality or severe morbidity.

Discussion

The present before-and-after study demonstrates that implementation of a comprehensive, multifaceted infection prevention bundle in a tertiary NICU was associated with significant reductions in overall HAI incidence (20.1% to 12.1%; adjusted OR 0.52), neonatal mortality (10.7% to 6.8%; adjusted OR 0.58), and device-associated infection rates, alongside substantial improvements in compliance with evidence-based prevention practices. These findings extend the growing evidence supporting bundled care interventions in neonatal populations ([7- 8].

The marked improvements across all 13 compliance indicators ranging from +18.4 percentage points for exclusive human milk feeding to +55.7 percentage points for monthly infection control feedback are concordant with the multi-centre quality improvement trials by [7- 9], who reported similar gains following structured bundle implementation. The 29.3-percentage-point increase in hand hygiene compliance aligns with the pooled 25–35% improvements reported in the systematic review by [10], while the 43.8-percentage-point gain in antibiotic stewardship adherence complements the findings of [11-12], who demonstrated that integrated stewardship reduces unnecessary antibiotic exposure and late-onset sepsis.

The 40% relative reduction in overall HAI and the 61.9% reduction in CLABSI rate (IRR 0.38) are consistent with, and in several instances exceed, reductions reported by [13] in the Vermont Oxford Network (28% reduction) and [14] in Dutch NICUs (65% CLABSI reduction). The 54% VAP reduction mirrors the 48% pooled reduction in the meta-analysis by [15]. However, the non-significant trends for urinary tract infection and invasive fungal infection likely reflect insufficient statistical power rather than true absence of effect, consistent with observations by [16].

The significant mortality reduction (36.4% relative decrease) is concordant with [17], who reported a 33% mortality reduction following a national HAI reduction programme in England. Importantly, the unchanged case-fatality rate among HAI-affected infants (28.6% vs. 28.4%) indicates that the mortality benefit was driven by prevention of infection acquisition rather than improved treatment of established infections, supporting the conclusions of [18] regarding the primacy of primary prevention. The significantly elevated rates of BPD (OR 2.01), severe IVH (OR 1.84), PVL (OR 1.89), and NEC (OR 2.14) among HAI-affected infants confirm the profound morbidity burden attributable to nosocomial infection, consistent with the meta-analysis by [19]. The nearly threefold increase in median NICU length of stay (58 vs. 32 days) and the 2.34-fold increase in re-hospitalisation risk carry substantial implications for healthcare resource utilisation, as quantified by [20].

Multivariate analyses identified prolonged mechanical ventilation (>7 days; OR 3.42) and central venous catheterisation

(>14 days; OR 2.87) as the strongest modifiable HAI risk factors, consistent with [21]. The independent protective effect of the post-intervention period (OR 0.48 for HAI; OR 0.62 for composite outcome) after adjustment for all confounders provides robust evidence that the bundle itself was responsible for the observed improvements. HAI emerged as the strongest independent predictor of the composite outcome of death or severe morbidity (OR 3.24), comparable to the OR of 3.1 reported by [22].

The principal limitations include the before and after design susceptible to temporal confounding, single centre setting, limited follow-up duration (18-24 months), and small event numbers for specific HAI subtypes. Nevertheless, the comprehensive assessment of 13 compliance indicators, validated surveillance definitions, and multivariate adjustment for key confounders strengthen the validity of our conclusions.

Conclusion

In conclusion, this study demonstrates that a multifaceted infection prevention bundle, encompassing hand hygiene, device care, environmental cleaning, antibiotic stewardship, nutritional support, and structured feedback, can achieve substantial and statistically significant reductions in HAI incidence, neonatal mortality, and major morbidity among preterm infants in a tertiary NICU. The 40% reduction in overall HAI, 36% reduction in mortality, and >50% reductions in CLABSI and VAP rates collectively affirm the transformative potential of systematic infection prevention in neonatal critical care. These findings contribute to the growing evidence base supporting the implementation of bundled care strategies as a standard of care in NICUs worldwide and underscore the ethical imperative to invest in prevention infrastructure for the most vulnerable hospitalised patients.

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