ORIGINAL RESEARCH ARTICLE

Comparative Analysis of Bilirubin, Liver Enzymes and Lactate Dehydrogenase in Neonates with Jaundice and Healthy Controls in Keffi, Nigeria.

Abstract

Background: Approximately 60% of full-term neonates experience jaundice due to increased bilirubin concentration. Jaundice is caused by increased serum bilirubin levels that accumulate in tissues, resulting from the destruction of red blood cells.
Objective: This study evaluated the biochemical alterations associated with full term neonates diagnosed with jaundice compared to healthy neonates in Keffi, Nasarawa State.
Study Design: An unmatched case-control study was conducted.
Methodology: Blood samples from 46 term neonates diagnosed with jaundice and 91 healthy neonates were analysed for bilirubin, liver enzymes and LDH levels following standard laboratory protocols. The data obtained were analysed using descriptive and inferential statistics, including independent t-tests, chi-square tests, ANOVA, and Pearson's correlation ($P<0.05$).

Results: Significantly elevated levels of total bilirubin (241.3 ± 108.5 µmol/L vs. 124.5 ± 35.1 µmol/L), direct bilirubin (80.2 ± 83.2 µmol/L vs. 33.2 ± 9.2 µmol/L), ALP (528.8 ± 385.5 IU/L vs. 231.4 ± 96.5 IU/L), AST (119.1 ± 222.7 IU/L vs. 21.7 ± 3.7 IU/L), ALT (107.4 ± 214.3 IU/L vs. 19.0 ± 4.3 IU/L), and LDH (722.2 ± 181.2 IU/L vs. 473.3 ± 174.0 IU/L) were observed in neonates with jaundice compared with controls ($P < 0.05$). Correlations were observed between bilirubin and LDH ($r = 0.68$) and between AST and LDH ($r = 0.61$), highlighting the interplay of haemolysis and hepatic stress.

Conclusion: The elevated levels of bilirubin, liver enzymes and lactate dehydrogenase in this study are significant. There is a need for early detection of these biomarkers in neonates especially in resource-limited settings.

Keywords: Bilirubin; lactate dehydrogenase; liver enzymes; Jaundice; Keffi and neonates.

Introduction

Hyperbilirubinemia in neonates, also known as jaundice, is a common condition in the neonatal period resulting from the adaptation of bilirubin metabolism that occurs during this phase of life (Aydin *et al*., 2016; Okulu, 2024). Although the condition is often harmless, acute bilirubin encephalopathy and kernicterus could result in neurological damage and may be fatal if left untreated or not properly managed (Usman *et al*., 2018; Rathore, 2019; Karimzadeh *et a*l., 2020). Jaundice is caused by increased serum bilirubin levels that accumulate in tissues, resulting from the destruction of red blood cells (RBCs). Bilirubin, in its indirect, unconjugated form, is transported in the circulation bound to serum albumin, resulting in a visible yellowish colouration of the skin and eyes (Hansen *et al*., 2020; Etukudoh *et al*., 2023; Verma & Singhal, 2024).

Slusher *et al*. (2011) reported that 667.8 per 100,000 live births in the African region, 251.3 per 100,000 live births in Southeast Asia and 3.7 per 100,000 live births in Europe experience severe neonatal jaundice. More recently, in a meta-analysis involving 84 articles, Diala *et al*. (2023) reported that 64 (76.19%) were from low- and lower-middle-income countries, and 14.26% of the studied neonates with jaundice in these studies had severe neonatal jaundice. The incidence of neonatal jaundice is not properly documented in resource-sparse regions (Bante *et al*., 2024). Nasarawa State is no exception in this regard; however, incidence ranging from 11.7% to 40.18% has been reported in parts of the country (Mbah *et al*., 2022; Etukudoh *et al*., 2023; Ochigbo *et al*., 2024). The biochemical parameters, total and direct bilirubin, ALT, AST, ALP, and LDH serve as critical indicators of erythrocyte destruction, hepatobiliary integrity, and overall neonatal metabolic status (Abdalwahab & Al-Hatemi, 2021; Hegyi & Kleinfeld, 2022).

By assessing these biochemicals in newborns with jaundice in Keffi, Nasarawa State, Nigeria, healthcare providers can better understand the severity of the disease and tailor treatments accordingly, ultimately contributing to the reduction of morbidity and mortality associated with this condition.

Materials and Methods

Study Area

The designated study area for this research is the Special Care Baby Unit (SCBU) of the Federal Medical Centre Keffi. As a tertiary hospital in the area, it provides critical care for neonates born in Keffi and the surrounding communities. Keffi is one of the 13 Local Government Areas in Nasarawa State, North Central Nigeria. Located about 47Km from the Federal Capital Territory (FCT), Abuja, Nigeria. It is situated between latitude 8^{o} 85^{o} North of the equator and longitude 7^{o} 87^{o} East of the meridian with an altitude of 850 meters above sea level (Figure 1) (Akwa *et al.,* 2007; Sufiyan *et al*., 2020). Moreover, a report from the 2006 National Population and Housing Census conducted by the Nigerian Population Commission estimated the total population of Keffi town at 92,550 with an annual growth rate of 5.2% (NPC, 2006).

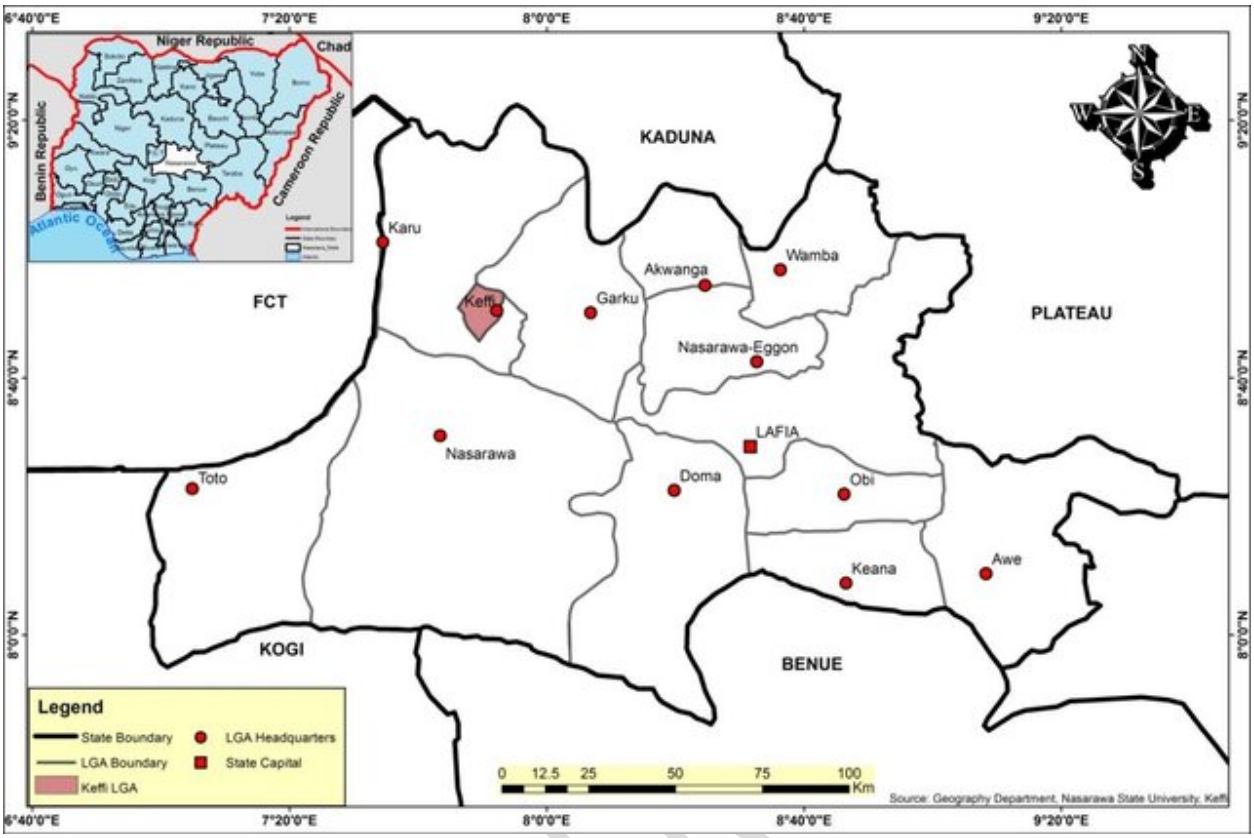

Fig. 1 Map of Nasarawa State (Abiola *et al.,* 2016).

Study Design

An unmatched case-control study was conducted among admitted neonates in the Special Baby Care Unit (SCBU) of Federal Medical Centre Keffi.

Study Population

Neonates diagnosed with jaundice at the Special Care Baby Unit of Federal Medical Centre Keffi, Nasarawa State, Nigeria, were recruited for this study.

Inclusion Criteria:

Neonates (0-28 days old) diagnosed with jaundice whose parents or guardians gave consent were recruited for this study.

Exclusion Criteria:

Neonates who were above 30 days after birth, who also had other congenital disorders and did not give consent were excluded.

Sample Size Determination

The minimum sample size for this study was determined using the formula for estimating a population proportion with a specified level of precision described by Sadiq *et al*. (2024).

$n0 = (Z^2 * p * q) / e^2$

Where:

- n0 = initial sample size
- Z = 1.96, corresponding to a 95% confidence interval
- p = 0.117 (11.7%), the estimated prevalence of haemolytic disease of the newborn in Nigeria (Etukudoh *et al*., 2023).
- q = 1 - p = 0.883
- e = 0.05, the desired margin of error

Substituting the values:

$n0 = (1.96^2 * 0.117 * 0.883) / (0.05^2) = 158.75 \approx 159$

Since the target population for the study was finite (N = 500), a finite population correction (FPC) was applied (Krejcie & Morgan, 1970).

$n = n0 / (1 + (n0 - 1)/N) = 158.75 / (1 + (158.75 - 1)/500) = 158.75 / 1.3155 \approx 121$

To account for a potential 10% non-response or drop-out rate**,** the sample size was adjusted:

$n\_adj = 121 / (1 - 0.10) = 121 / 0.9 \approx 135$

Therefore, the final sample size for the study was 135 participants.

The study design required a case-control ratio of 1:2 (Jaundice cases: non-jaundice controls). The total sample of 135 participants was divided as follows:

Total parts = 1 + 2 = 3

- Cases = 1/3 × 135 = 45
- Controls = 2/3 × 135 = 90 (Zeleke *et al.*, 2025).

The figure was rounded up to 137 to get a balanced ratio of 46:91 cases and controls, respectively.

That is 1:2 (Cases: Controls). Based on this, our calculated sample size was 46 cases and 91 controls.

Collection and processing of blood samples.

Blood samples (5 ml) were collected from patients and controls using vacutainers into plain labelled containers. They were allowed to clot and retract. They were then centrifuged at 3,000 revolutions per second. The serum obtained was transferred into sterile plain containers and then labelled appropriately. These were then stored frozen at -20 degrees Celsius until needed for analysis. Bilirubin (Direct and Total) was estimated by the Jendrassik-Grof method, AST, ALT, ALP and LDH levels were determined by the IFCC method using DiaLab reagents (DiaLab Austria) with the fully automated ChemWell 2902 Bichemistry Analyser (Awareness Technologies, USA).

Statistical Analysis

Descriptive Statistics was used for the Mean ± Standard Deviation (SD) to summarise biochemical parameters (bilirubin, AST, ALT, ALP, LDH) for both jaundice cases and controls. Frequencies and percentages were used to present demographic variables (e.g., sex, age distribution).

An Independent Samples t-test was applied to compare the mean values of biochemical parameters between the cases and controls. One-Way Analysis of Variance (ANOVA) was used to compare mean biochemical values across different age categories of neonates (1-5 days, 6-10 days, >10 days). Pearson's Correlation Coefficient (r) was used to assess the relationship between bilirubin levels and liver enzymes and LDH. Statistical significance was set at $p < 0.05$.

Results

The demographic characteristics of the study participants.

The participants were grouped based on age and gender (Table 1). The majority were between 6-10 days old (33.6%), followed by 1-5 days (27.0%) and 11-15 days (21.9%). The gender distribution indicated a higher proportion of males (56.2%) compared to females (43.8%).

Table 1. Demographic Characteristics of Study Participants by Age and Gender

Variable	Frequency (N = 137)	Percentage (%)
Age (In days)		
1-5	37	27.0
6-10	46	33.6
11-15	30	21.9
Gender		
Female	60	43.8
Male	77	56.2

The relationship between age in days and total bilirubin levels

This scatter plot (Figure 2) shows the relationship between age in days (x-axis) and total bilirubin levels (µmol/L) (y-axis). Each point represents an individual measurement. The regression line indicates a negative correlation (slope = –5.2836), meaning total bilirubin levels tend to decrease as the age of the neonates increases. The intercept (216.32) suggests that bilirubin levels are highest shortly after birth and decline gradually over the first 30 days of life.

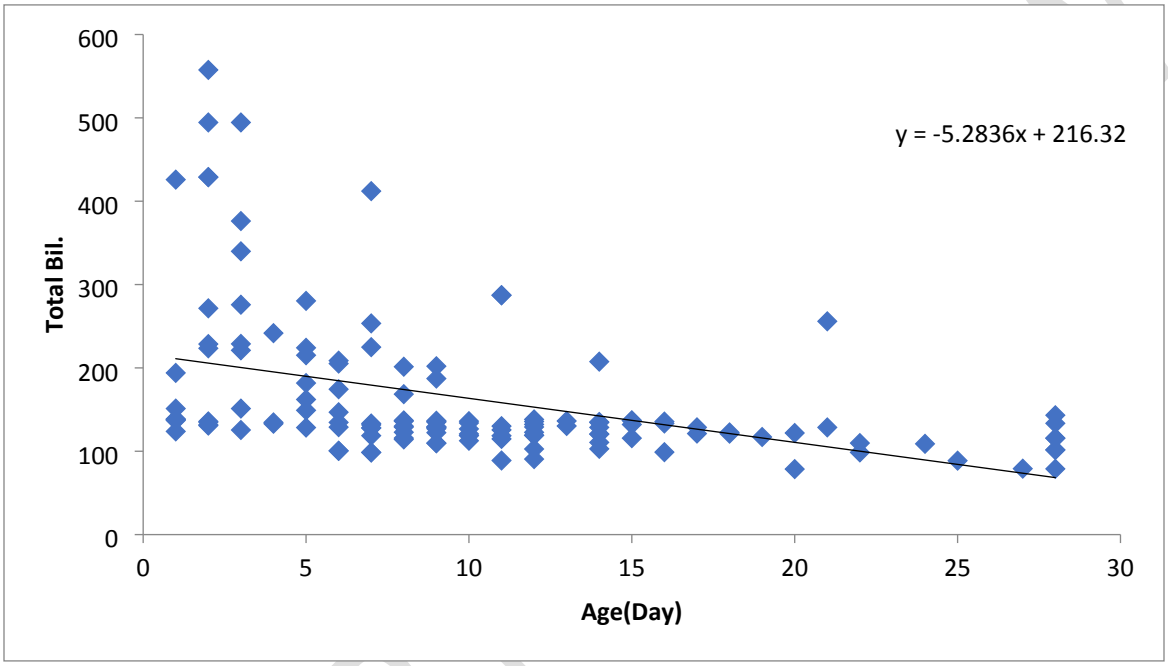

Figure 2. Relationship between Age (Days) and Total Bilirubin

The relationship between age in days and direct bilirubin levels

This scatter plot (Figure 3) illustrates the relationship between age in days (x-axis) and direct bilirubin levels (µmol/L) (y-axis). The data points show the distribution of bilirubin values across the ages, represented in days. The regression line reveals a negative trend (slope = –1.7736), indicating that direct bilirubin levels decrease as age increases. The intercept (66.625) suggests relatively higher direct bilirubin levels in the early neonatal period, followed by a gradual decline with age.

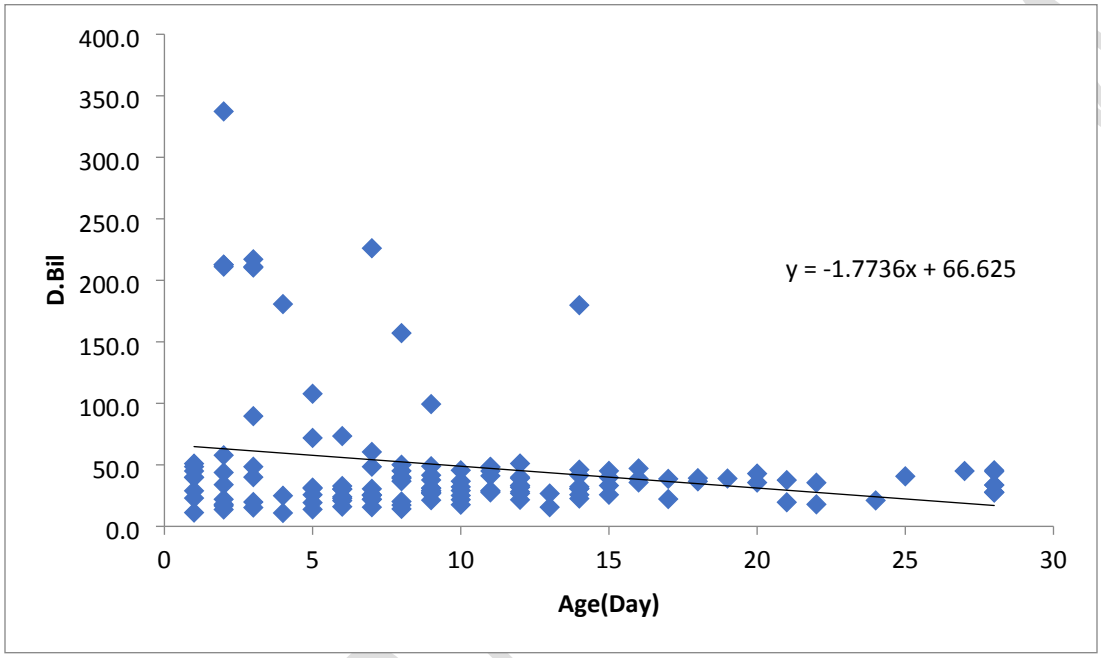

Figure 3. Relationship between Age (Days) and Direct Bilirubin

Comparison between the mean values of biochemical parameters between cases and controls.

The results show that participants with jaundice had significantly higher levels of total bilirubin, direct bilirubin, ALP, AST, ALT, and LDH compared to control participants, even though the mean age of cases was significantly lower than that of controls ($P < 0.05$) (Table 2). These findings indicate marked biochemical alterations associated with the condition under study.

Table 2. Comparison of Biochemical Parameters Between Cases and Controls

Parameter	Cases (Mean ± SD)	Controls (Mean ± SD)	t-value	p-value
Age (Days)	5.96 ± 5.06	12.16 ± 6.96	-5.955	<0.001
Total Bilirubin (µmol/L)	241.28 ± 108.46	124.46 ± 35.10	7.121	<0.001
Direct Bilirubin (µmol/L)	80.22 ± 83.18	33.24 ± 9.20	3.819	0.0001
ALP (U/L)	528.84 ± 385.52	231.43 ± 96.54	5.152	<0.001
AST (U/L)	119.13 ± 222.73	21.73 ± 3.69	2.966	0.0030
ALT (U/L)	107.38 ± 214.26	18.98 ± 4.27	2.798	0.0051
LDH (U/L)	722.20 ± 181.20	473.30 ± 174.00	7.707	<0.001

Alkaline Phosphatase (ALP); Alanine Aminotransaminase (ALT); Aspartate Transaminase (AST); Lactate Dehydrogenase (LDH) and Units per litre (UL).

Correlation between LDH and selected biochemical parameters.

A significant positive correlation was observed between LDH and AST ($r = 0.382$, $P < 0.05$), while no significant correlations were found between LDH and ALP or ALT ($P > 0.05$) (Table 3).

Table 3. Correlation between LDH and Selected Biochemical Parameters in Cases

Biochemical parameters	Correlation with LDH (r-value)	P-value
ALP (U/L)	0.104	0.495
AST (U/L)	0.382	0.010
ALT (U/L)	0.263	0.081
LDH (U/L)	0.388	0.008

Alkaline Phosphatase (ALP); Alanine Aminotransaminase (ALT); Aspartate Transaminase (AST); Lactate Dehydrogenase (LDH) and Units per litre (UL).

Correlation between bilirubin and selected biochemical parameters.

Both total and direct bilirubin demonstrated significant positive correlations with AST, ALT, and LDH, with the strongest correlation observed between direct bilirubin and LDH ($r = 0.657$, $P < 0.05$). No significant correlation was found between bilirubin (total or direct) and ALP ($P > 0.05$) (Table 4).

Table 4. Correlation Between Bilirubin (Total and Direct) and Selected Biochemical Parameters in Cases

Biochemical Parameter	Total Bilirubin (r-value)	p-value	Direct Bilirubin (r-value)	p-value
ALP (U/L)	0.202	0.183	0.230	0.129
AST (GOT) (U/L)	0.423	0.004	0.454	0.002
ALT (GPT) (U/L)	0.349	0.019	0.318	0.034
LDH (U/L)	0.388	0.008	0.657	0.000

Comparison of biochemical parameters across different neonatal age groups.

Significant differences were observed for total bilirubin, direct bilirubin, ALP, AST, and LDH ($P < 0.05$), with the highest values generally recorded within the 1-5 days age group. However, ALT showed no significant variation across the age categories (Table 5).

Table 5. Comparison of Biochemical Parameters Across Different Age Groups of Participants

Parameter	1–5 Days *Mean* ± *SD*	6–10 Days *Mean* ± *SD*	11–15 Days *Mean* ± *SD*	16–20 Days *Mean* ± *SD*	≥21 Days *Mean* ± *SD*	F-value	P-value
Total Bilirubin (µmol/L)	234.50 ± 124.03	145.69 ± 53.29	136.35 ± 45.74	118.80 ± 16.54	117.80 ± 45.52	11.670	0.000
Direct Bilirubin (µmol/L)	76.65 ± 83.78	39.79 ± 36.97	38.92 ± 28.07	37.55 ± 6.09	32.33 ± 9.71	3.926	0.005
ALP (U/L)	422.87 ± 367.65	368.15 ± 280.80	256.95 ± 130.68	224.35 ± 110.60	179.43 ± 72.67	3.495	0.010
AST (GOT) (U/L)	124.40 ± 246.58	30.87 ± 18.75	23.58 ± 10.39	21.66 ± 2.89	30.09 ± 26.04	3.793	0.006
ALT (GPT) (U/L)	100.11 ± 231.65	28.97 ± 21.34	31.02 ± 73.96	20.38 ± 3.22	29.64 ± 25.58	2.158	0.077
LDH (U/L)	690.40 ± 210.58	567.47 ± 187.43	458.55 ± 171.85	456.93 ± 184.40	431.89 ± 189.66	8.704	0.000

Discussion

This study evaluated biochemical parameters in neonates with jaundice in Keffi, Nasarawa State, and compared them with age-matched controls. The results revealed significantly elevated levels of total and direct bilirubin, alkaline phosphatase (ALP), aspartate transaminase (AST), alanine transaminase (ALT), and lactate dehydrogenase (LDH) in jaundice-affected neonates compared to controls ($P < 0.05$). Strong correlations were observed between bilirubin levels and hepatic enzymes, as well as LDH, underscoring the interplay between haemolysis and hepatic stress in neonatal jaundice.

Hyperbilirubinemia was most pronounced in neonates aged 1-5 days, after which values declined with age. This reflects the natural peak of haemolysis and bilirubin production in the immediate neonatal period. By the second week of life, most parameters had declined significantly, suggesting treatment response and hepatic adaptation. This pattern is consistent with findings by Mitra & Rennie (2017). The persistence of elevated LDH despite bilirubin decline highlights its role in detecting ongoing haemolysis even after clinical improvement (Piel & Musallam, 2018).

The significantly higher total and direct bilirubin levels among neonates with jaundice confirm that hyperbilirubinemia is the hallmark of haemolysis in neonates. The mean total bilirubin among cases (241.3 µmol/L) was nearly double that of controls (124.5 µmol/L), while direct bilirubin also rose markedly. This pattern reflects accelerated haem breakdown and immature hepatic conjugation mechanisms (Yadav *et al*., 2018; Liu *et al*., 2021). Elevated conjugated bilirubin suggests cholestatic stress in some infants, consistent with previous studies that linked it with conjugated hyperbilirubinemia (Fawaz *et al*., 2017; Karpen, 2020).

Similar findings were reported in Southwest Nigeria, showing neonates with jaundice exhibited bilirubin values exceeding 200 µmol/L (Osuorah *et al*., 2018). Elevated levels of bilirubin have also been reported in other regions of Africa (Aynalem *et al*., 2020; Nassuna *et al*., 2022; Bakari *et al*., 2025). A correlation between increased serum bilirubin and liver enzymes was reported among neonates with physiological and pathological jaundice in Iraq by Kamal & Hassan (2021). Similarly, Saboute *et al.* (2022) reported increased levels of ALP and bilirubin among neonates with jaundice compared to the control cases. If not controlled, high levels of bilirubin increase the risk of complications, emphasising the clinical importance of early monitoring and intervention (Zhang, 2018; Bante *et al.*, 2024).

The elevation of liver enzymes observed in this study underscores hepatic involvement in jaundice. AST values in neonates with jaundice (119.1 IU/L) were fivefold higher than those of controls (21.7 IU/L), while ALT values were also significantly elevated. AST showed stronger correlations with bilirubin and LDH than ALT, reflecting its dual release from hepatocytes and erythrocytes (Chhavi *et al*., 2022). This makes AST a more sensitive indicator of both haemolysis and hepatic stress. ALT elevation, though less pronounced, is significant as it indicates direct hepatocellular injury from bilirubin overload and inflammatory stress (Kapur *et al*., 2014; Kariya *et al*., 2020). Elevated ALP values in neonates with jaundice (528.8 IU/L vs. 231.4 IU/L in controls) suggest cholestatic obstruction or hepatic immaturity. Saboute *et al*. (2022) reported similar elevations in Iranian neonates, noting that they did not find a correlation between ALP levels and pathological jaundice in patients. Abdalwahab & Al-Hatemi (2021) reported a similar increase in ALT and ALP levels but with a decrease in AST levels among neonates with jaundice in Romania. On the contrary, Liu *et al*. (2021) and Yousefi *et al.* (2025) reported normal levels of ALP.

LDH levels were significantly elevated in neonates with jaundice compared with controls (722.2 vs. 473.3 IU/L). LDH is a well-established marker of haemolysis since it is released in large amounts from lysed red blood cells (Ariyibi *et al*., 2024). The positive correlation with bilirubin and AST observed in this study strengthens its diagnostic and prognostic value.

Liu *et al*. (2023) reported high levels of LDH in Asian cohorts, where LDH was a better predictor of disease severity than bilirubin alone. This supports the use of LDH as a severity marker, particularly where advanced diagnostic tools are unavailable.

Conclusion

The current study observed that jaundice in neonates in Keffi is associated with profound biochemical changes involving bilirubin metabolism, liver enzyme activity, and haemolysis markers. High levels of bilirubin, AST, ALT, ALP, and LDH provide a comprehensive biochemical picture of the disease process, with LDH serving as an especially sensitive indicator of severity. The results confirm a high incidence of jaundice in the study area and its propensity to cause significant neonatal morbidity and mortality. Furthermore, these relatively simple biochemical tests can serve as effective diagnostic and monitoring tools in resource-limited settings. In comparison with other studies from Nigeria, West Africa, and globally, the findings are consistent with the recognised pathophysiological patterns of jaundice. The study highlights the need for more awareness. In addition, governments at all levels should prioritise the provision of the necessary infrastructure and funding for neonatal care.

Limitations

This study did not determine the cause of jaundice and the treatment outcomes of the disease among the participants.

Consent

Consent to participate in this study was obtained in writing from all subjects after explaining the entire research protocol and justification to them in a language they understand.

Ethical Approval

Ethical approval was obtained from the Health Research Ethics Committee of the Nasarawa State Ministry of Health (NHREC Protocol Number: 18/06/2017).

Disclaimer (Artificial intelligence)

Option 1:

Author(s) hereby declare that NO generative AI technologies such as Large Language Models (ChatGPT, COPILOT, etc.) and text-to-image generators have been used during the writing or editing of this manuscript.

References

Abdalwahab, W. I. A., & Al-Hatemi, A. S. J. (2021). Physiochemical effect of neonatal jaundice on some liver enzymes and cholecystokin in hormone. *Annals of the Romanian Society for Cell Biology*, *25*(6), 2912-2917.http://annalsofrscb.ro/index.php/journal/article/view/5988

Abiola, K. A., Medugu, N. I., Kadafa, A. A. & Opaluwa, O. D. (2016). Heavy metal contamination of top soil at the vehicles workshop in Keffi Town, Nasarawa State. IOSR *Journal of Environmental Science, Toxicology and Food Technology*, 10(08), 84-87. https://doi.org/10.9790/2402-1008028487

Akwa, V. L., Binbol, N. L., Samaila, K. L., & Marcus, N. D. (2007). Keffi. In *Geographical perspective of Nasarawa State* (p. 503). Onaive Printing and Publishing Company Ltd.

Ariyibi, S., Ojuawo, A., Adesiyun, O., Adebara, O., Ogunwale, K., Ojuawo, A., Ray, E., & Sanusi, I. (2024). Predictive value of cord blood concentrations of selected hepatic enzymes in Hypoxic-Ischaemic encephalopathy and related mortality. *Annals of Health Research (the Journal of the Medical and Dental Consultants Association of Nigeria OOUTH Sagamu Nigeria)*, *10*(4), 323–331. https://doi.org/10.30442/ahr.1004-01-252

Aydın, M., Hardalaç, F., Ural, B., & Karap, S. (2016). Neonatal Jaundice Detection System. Journal of medical systems, 40(7), 166. https://doi.org/10.1007/s10916-016-0523-4

Aynalem, Y. A., Mulu, G. B., Akalu, T. Y., & Shiferaw, W. S. (2020). Prevalence of neonatal hyperbilirubinaemia and its association with glucose-6-phosphate dehydrogenase deficiency and blood-type incompatibility in sub-Saharan Africa: a systematic review and meta-analysis. *BMJ paediatrics open*, *4*(1), e000750. https://doi.org/10.1136/bmjpo-2020-000750

Bakari, A., Wolski, A. V., Otoo, B., Amoah, R., Kaselitz, E., Compton, S. D., & Shaw, R. (2025). Neonatal jaundice Treatment versus recommendations: The challenge of treatment without rapid diagnostic capability. *International Journal of Environmental Research and Public Health*, *22*(7), 1032. https://doi.org/10.3390/ijerph22071032

Bante, A., Ahmed, M., Degefa, N., Shibiru, S., & Yihune, M. (2024). Neonatal jaundice and associated factors in public hospitals of southern Ethiopia: A multi-center cross-sectional study. *Heliyon*, *10*(2), e24838. https://doi.org/10.1016/j.heliyon.2024.e24838

Barcellini, W., & Fattizzo, B. (2023). Strategies to overcome the diagnostic challenges of autoimmune hemolytic anemias. Expert review of hematology, 16(7), 515–524. https://doi.org/10.1080/17474086.2023.2216930

Chhavi, N., Ojha, S., Awasthi, A., Shalimar, & Goel, A. (2022). Serum Level of Alanine- and Aspartate-Aminotransferase Levels in Newborns in India. *Journal of clinical and experimental hepatology*, *12*(2), 306–311. https://doi.org/10.1016/j.jceh.2021.08.024

Diala, U. M., Usman, F., Appiah, D., Hassan, L., Ogundele, T., Abdullahi, F., & Satrom, K. M. (2023). Global Prevalence of Severe Neonatal Jaundice among Hospital Admissions: A Systematic Review and Meta-Analysis. *Journal of Clinical Medicine*, *12*(11), 3738. https://doi.org/10.3390/jcm12113738

Etukudoh, N. S., Obeta, U. M., Garang, M. J., Ejinaka, O. R., Ibanga, I., & Kuruyang, T. A. (2023). Prevalence and management of neonatal jaundice in a hospital, Jos-Nigeria. *Journal of Public Health and Diseases*, *6*(1), 10–14. https://doi.org/10.31248/jphd2023.125

Fawaz, R., Baumann, U., Ekong, U., Fischler, B., Hadzic, N., Mack, C. L., & McLin, V. A. (2017). Guideline for the Evaluation of Cholestatic Jaundice in Infants: Joint Recommendations of the North American Society for Pediatric Gastroenterology, Hepatology, and Nutrition and the European Society for Pediatric Gastroenterology, Hepatology, and Nutrition. *Journal of Pediatric Gastroenterology and Nutrition*, *64*(1), 154-168.https://doi.org/10.1097/MPG.0000000000001334

Hansen, T. W. R., Wong, R. J., & Stevenson, D. K. (2020). Molecular Physiology and Pathophysiology of Bilirubin Handling by the Blood, Liver, Intestine, and Brain in the Newborn. Physiological Reviews, 100(3), 1291-1346. https://doi.org/10.1152/physrev.00004.2019

Hegyi, T., & Kleinfeld, A. (2022). Neonatal hyperbilirubinemia and the role of unbound bilirubin. The Journal of Maternal-Fetal & Neonatal Medicine: The official journal of the European Association of Perinatal Medicine, the Federation of Asia and Oceania Perinatal Societies, the International Society of Perinatal Obstetricians, 35(25), 9201–9207. https://doi.org/10.1080/14767058.2021.2021177

Kamal, A. N., & Hassan, A. F. (2021). Comparative Study of Liver Function and Rh Blood Group between both Physiological and Pathological Neonatal Jaundice. *Iraqi Journal of Pharmaceutical Sciences (P-ISSN 1683 – 3597 E-ISSN 2521 – 3512)*, *30*(1), 101–109. https://doi.org/10.31351/vol30iss1pp101-109

Kapur, R., Della Valle, L., Sonneveld, M., Hipgrave Ederveen, A., & Visser, R. (2014). Low anti-RhD IgG-Fc-fucosylation in pregnancy: a new variable predicting severity in haemolytic disease of the fetus and newborn. *British journal of haematology*, *166*(6), 936–945. https://doi.org/10.1111/bjh.12965

Karimzadeh, P., Fallahi, M., Kazemian, M., Taslimi Taleghani, N., Nouripour, S., & Radfar, M. (2020). Bilirubin Induced Encephalopathy. *Iranian journal of child neurology*, *14*(1), 7–19.

Kariya, V., Jain, M., & Jategaonkar, S. (2020). Study of hepatic enzymes in term neonates with perinatal asphyxia. Journal of Clinical Neonatology, 9(2), 125–131. https://doi.org/10.4103/jcn.JCN_116_19

Karpen S. J. (2020). Pediatric Cholestasis: Epidemiology, Genetics, Diagnosis, and Current Management. *Clinical liver disease*, *15*(3), 115–119. https://doi.org/10.1002/cld.895

Krejcie, R. V., & Morgan, D. W. (1970). Determining sample size for research activities. *Educational and Psychological Measurement, 30*(3), 607–610.

Liu, X., Dong, Y., Qin, Y., Xue, C., & Lyu, W. (2023). Clinical value of combined predictors of RET%, γ-GT, LDH in the ABO neonatal hemolytic disease. *Frontiers in pediatrics*, *11*, 1265739. https://doi.org/10.3389/fped.2023.1265739

Liu, Y., Sun, X., Wang, Y., Xing, C., Li, L., & Zhou, S. (2021). Evaluation of Associated Markers of Neonatal Pathological Jaundice Due to Bacterial Infection. *Iranian Journal of Public Health*, *50*(2), 333–340. https://doi.org/10.18502/ijph.v50i2.5394

Mbah, M. I., Emmanuel, H., Samari, M. S., & Boshi, B. T. (2022). Incidence and risk factors to neonatal jaundice in Jalingo, Taraba State. *Journal of Biosciences and Medicines*, *10*(10), 152–163. https://doi.org/10.4236/jbm.2022.1010012

Mitra, S., & Rennie, J. (2017). Neonatal jaundice: aetiology, diagnosis and treatment. *British journal of hospital medicine (London, England: 2005)*, *78*(12), 699–704. https://doi.org/10.12968/hmed.2017.78.12.699

Nassuna, C., Yaser, A., Karamagi, C., & Mugalu, J. (2022). Significant hyperbilirubinemia among well neonates due for discharge at Kawempe-Mulago Hospital, prevalence, factors associated, and accuracy of transcutaneous bilirubinometry for screening. *African health sciences*, *22*(2), 526–534. https://doi.org/10.4314/ahs.v22i2.61

National Population Commission (NPC) (2006) Nigeria National Census: Population Distribution by Sex, State, LGAs and Senatorial District: 2006 Census Priority Tables (Vol. 3). http://www.population.gov.ng/index.php/publication/140-popn-distri-by-sex-state-jgas-and-senatorial-distr-2006

Ochigbo, S., Ekpebe, P., Nyong, E. E., Ikechukwu, O., Ibeawuchi, A., Eigbedion, A., & Adeyemi, O. O. (2024). Neonatal jaundice incidence, risk factors and outcomes in referral-level facilities in Nigeria. *BJOG: an international journal of obstetrics and gynaecology*, *131*(Suppl 3), 113–124. https://doi.org/10.1111/1471-0528.17865

Okulu, E. (2023). Neonatal jaundice: Recommendations for follow-up and treatment. Global Pediatrics, 7, 100131. https://doi.org/10.1016/j.gpeds.2023.100131

Osuorah, C. D. I., Ekwochi, U., & Asinobi, I. N. (2018). Clinical evaluation of severe neonatal Hyperbilirubinaemia in a resource-limited setting: a 4-year longitudinal study in south-East Nigeria. *BMC Pediatrics*, *18*(1). https://doi.org/10.1186/s12887-018-1174-z

Rathore, S., Vk, C. K., & R, S. (2019). A critical review on neonatal hyperbilirubinemia-an Ayurvedic perspective. *Journal of Ayurveda and Integrative Medicine*, *11*(2), 190–196. https://doi.org/10.1016/j.jaim.2018.08.006

Saboute, M., Mahmoudian, A., Khalesi, N., Vahedi, Z., Khosravi, N., & Allahqoli, L. (2022). Correlation between Alkaline Phosphatase and Neonatal Jaundice. Medical journal of the Islamic Republic of Iran, 36, 52. https://doi.org/10.47176/mjiri.36.52

Sadiq, I. Z., Usman, A., Muhammad, A., & Ahmad, K. H. (2024). Sample size calculation in biomedical, clinical and biological sciences research. Journal of Umm Al-Qura University for Applied Sciences. https://doi.org/10.1007/s43994-024-00153-x

Slusher, T. M., Zipursky, A., & Bhutani, V. K. (2011). A global need for affordable neonatal jaundice technologies. *Seminars in Perinatology*, *35*(3), 185-191.https://doi.org/10.1053/j.semperi. 2011.02.014

Sufiyan, I., Mohammed, K., Bello, I., & Zaharadeen, I. (2020). Impact of Harmattan Season on Human Health in Keffi, Nasarawa State, Nigeria. Matrix Science Medica, 4(2), 44. https://doi.org/10.4103/mtsm.mtsm_1_20

Usman, F., Diala, U., Shapiro, S., Pichon, J. L., & Slusher, T. (2018). Acute bilirubin encephalopathy and its progression to kernicterus: current perspectives. *Research and Reports in Neonatology*, *Volume 8*, 33–44. https://doi.org/10.2147/rrn.s125758

Verma, D. K., & Singhal, H. K. (2024). A Critical analysis of Neonatal jaundice: the synergy of Ayurveda and phototherapy. *International Journal of Science and Research (IJSR)*, *13*(10), 1368–1374. https://doi.org/10.21275/sr241017143422

Yadav, K. P., Yadav, M. K., Yadav, R., Mohapatra, T. K., Mohapatra, R. K., & Mishra, P. K. (2018). Comparative study of the serum bilirubin and various other liver-related enzymes in different types of jaundice. *Annals of International Medical and Dental Research*, *4*(4), BC42–BC46.

Yousefi, R., Shojaie, S., & Yousefi, M. (2025). Prolonged jaundice in newborns is a common condition that affects many infants: A case study. *Journal of Nursing Reports in Clinical Practice*, *3*(6), 616–620. https://doi.org/10.32598/jnrcp.2502.1240

Zeleke, B. A., Ersado, T. L., Hanjelo, H. W., & Zeleke, G. A. (2025). Determinants of neonatal jaundice among neonates admitted to neonatal intensive care unit in hospitals of Gurage zone, Southern Ethiopia. *BMC pediatrics*, *25*(1), 427. https://doi.org/10.1186/s12887-025-05772-9

Zhang, L. (2018). Severe neonatal hyperbilirubinemia induces temporal and occipital lobe seizures. *PLoS ONE*, *13*(5), e0197113. https://doi.org/10.1371/journal.pone.0197113