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Clinical Burden of Dengue Fever and On-Admission Atypical Lymphocyte Count as a Prognostic Biomarker – A Case Study

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ABSTRACT

Dengue fever imposes a substantial economic burden on healthcare systems, particularly in low- and middle-income countries. This study aimed to assess the financial impact of dengue fever in a private hospital setting in Sri Lanka and to evaluate the predictive value of on-admission atypical lymphocyte count (ALC) for disease severity, length of hospital stay, and total hospital costs. A retrospective analysis was conducted on 2,185 confirmed dengue patients admitted to Nawaloka Hospital, Colombo, between January 2017 and August 2023. Data on patient demographics, disease severity (per WHO 2009 classification), financial records, and ALC values from the Sysmex XS500i analyzer were extracted. The median total hospital bill was LKR 127,600, with room charges and administrative costs contributing the most. Severe dengue, prolonged hospitalization (>5 days), and insurance coverage were significantly associated with higher hospital bills ($p<0.001$). Patients with an ALC $>0.5\times10^3/\mu L$ on day 3 of fever had significantly longer hospital stays and higher costs compared to those with lower ALC levels. ROC analysis showed that elevated ALC predicted hospital stays >5 days with 94.4% sensitivity and 78.4% specificity, and costs >LKR 132,000 with 95.8% sensitivity and 72.4% specificity. These findings highlight ALC as a practical, early biomarker to stratify dengue patients by risk and optimize resource allocation. The study underscores the need for early clinical decision-making

to minimize economic strain on patients, especially those lacking insurance coverage. Further prospective research is recommended to validate ALC as a cost-saving predictive tool in dengue management.
Keywords: Dengue, Out of pocket, financial, atypical lymphocyte.

1 Introduction

Dengue infection (DI) is the most prevalent arthropod-borne viral illness globally, with an estimated 2.5 billion people at risk across endemic regions (Guzman et al., 2010, WHO 2023). The clinical spectrum of dengue is highly variable, ranging from asymptomatic or mild febrile illness to severe and potentially fatal complications such as dengue hemorrhagic fever (DHF) and dengue shock syndrome (DSS) (Huy et al., 2013, WHO 2009). Although only 2–5% of patients develop severe forms of the disease, early identification of at-risk individuals is essential for effective triage, optimized care, and efficient resource utilization, especially in low- and middle-income countries (Jaenisch et al., 2016).

The economic burden of dengue is significant and multifaceted, encompassing both direct medical costs and indirect productivity losses (Shepard et al., 2016). Several studies in Sri Lanka have documented hospitalization costs in the public sector (Sigera et al., 2021, Shrestha et al., 2022) yet there remains a paucity of data from private hospitals where overhead charges and out-of-pocket expenditures are considerably higher.

No laboratory test currently reliably predicts the severity of dengue infection. Although clinical signs such as abdominal pain, vomiting, hepatomegaly, and fluid accumulation are used as warning indicators (Kalayanarooj, 2011), their subjective nature limits predictive accuracy (Naghavi et al., 2015). Atypical lymphocyte count (ALC) obtained via automated full blood count (FBC) analyzers has emerged as a potential biomarker due to its sensitivity to immunological changes in viral infections (Seo et al., 2015). Preliminary research suggests ALC may correlate with dengue severity and thrombocytopenia (Abeysuriya et al., 2020).

This study was undertaken to evaluate the financial burden of dengue fever in a private tertiary care setting in Sri Lanka and to assess the utility of on-admission ALC as an early predictor of disease severity, length of hospitalization, and total treatment cost.

2 Methodology

2.1 Study Design and Setting

This retrospective cohort study was conducted at Nawaloka Hospital, a leading private healthcare institution in Colombo, Sri Lanka. As this was a single-center study conducted in a private hospital, the findings may not be fully generalizable to the wider Sri Lankan population, particularly patients treated

in the public sector where socioeconomic and insurance profiles differ. Data were collected for all patients admitted with a confirmed diagnosis of dengue infection (DI) between January 2017 and August 2023.

2.2 Source of data

Clinical and demographic data were extracted from the hospital's electronic medical records system. Financial data, including itemized hospital charges, were retrieved from the computerized billing system maintained by the hospital. All hospital costs from 2017–2023 were adjusted to constant 2023 LKR values using the national annual inflation index (Department of Census and Statistics, Sri Lanka). USD conversions were calculated only for inflation-adjusted 2023 costs, ensuring valid cross-study comparisons. Laboratory parameters, specifically Atypical Lymphocyte Count (ALC), were obtained from the Sysmex XS500i automated Full Blood Count (FBC) analyzer (Sysmex Corporation, Kobe, Japan). Patients with missing ALC values were excluded from the analysis to maintain internal validity. ALC was measured on hospital admission, which consistently occurred on day 3 of fever in this cohort, as patients typically presented at this time point.

2.3 Sampling Scheme and Study Population

A total of 2,258 patients aged between 1 and 90 years were included in the study. Inclusion criteria were patients with a confirmed diagnosis of dengue infection through either a positive non-structural antigen 1 (NS1) test or dengue immunoglobulin M (IgM) antibody. Patients with hematologic malignancies, immunosuppressive conditions, HIV-positive status, or co-infection with other viral pathogens were excluded based on diagnostic records.

2.4 Variables and Definitions

Dengue Classification: Patients were categorized based on the World Health Organization 2009 guidelines into (i) dengue without warning signs, (ii) dengue with warning signs, and (iii) severe dengue.

ALC Count: On-admission ALC was defined as the count measured on the third day of fever onset. An ALC $> 0.5 \times 10^3/\mu L$ was considered elevated, based on existing literature (Abeysuriya et al., 2020). This threshold was selected based on prior literature, but to further evaluate its validity, we performed ROC-based threshold optimization, which confirmed $0.5 \times 10^3/\mu L$ as the most discriminative cutoff in this dataset. Nonetheless, the reliance on a single threshold should be interpreted with caution, and prospective validation in larger, multicenter studies is warranted.

Financial Variables: The total hospital bill was disaggregated into costs for (i) laboratory investigations, (ii) intravenous fluids and medications, (iii) imaging (ultrasound, X-ray, ECG, ECHO), and (iv) room and administrative charges.

2.5 Data Analysis

Data was entered and cleaned using Microsoft Excel. As the financial variables were skewed, non-parametric statistical methods were used. Descriptive statistics included medians and interquartile ranges (IQRs). The Mann-Whitney U test and Kruskal-Wallis test were used for between-group comparisons. Linear regression analysis was performed to assess predictors of total hospital bill and hospital length of stay. Assumptions of regression analysis were checked. Normality of residuals was assessed with the Shapiro-Wilk test and Q-Q plots. Homoscedasticity was evaluated by plotting residuals against fitted values. Outliers were examined using Cook's distance. Due to skewed cost data, log-transformation was considered; however, non-parametric tests were primarily used for group comparisons. Age was included as a covariate in regression models. However, data on co-morbidities and seasonal variation were not available in this retrospective dataset and could not be included in multivariate models. Receiver Operating Characteristic (ROC) curve analysis was conducted to evaluate the predictive value of ALC ($>0.5 \times 10^3/\mu L$) for extended hospital stay (>5 days) and higher hospital cost (>LKR 132,000). Statistical analyses were performed using SPSS version 20.0 (Chicago, IL, USA) and STATA version 17 (Texas, USA). A p-value < 0.05 was considered statistically significant. Alternative thresholds (e.g., median or 90th percentile) were considered but not formally tested. Sensitivity analyses across different cost thresholds were beyond the scope of this study.

2.6 Ethical Approval

Ethical approval for this study was obtained from the Ethics Review Committee of Nawaloka Hospitals Research and Education Foundation (NHREF).

3 Results

A total of 2,258 patients with clinically confirmed dengue were admitted to the study hospital during 2017–2023. Of these, 73 were excluded due to missing atypical lymphocyte count (ALC) values (n = 49), incomplete records (n = 21), or serologically unconfirmed diagnosis (n = 03). The final study cohort comprised 2,185 patients who were included in the statistical analysis. (Figure 1)

Table 1 shows the socio-demographic characteristics of the study population. Female patients were slightly more dominant (N = 1,135; 51.9%). The most prominent age category was adults aged 25–44 years (34.4%), followed by adolescents aged 15–24 years (23.0%). Children below 15 years represented 16.9% of the study population, while middle-aged patients (45–59 years) accounted for 21.5%, and elderly patients aged ≥60 years comprised 4.2%. More than half of the sample (57.4%) were covered by an insurance scheme. Dengue without warning signs was the most common clinical group (84.9%), while severe dengue was diagnosed in 3.4% of patients. The majority of patients (82.2%) had a hospital stay of less than 5 days.

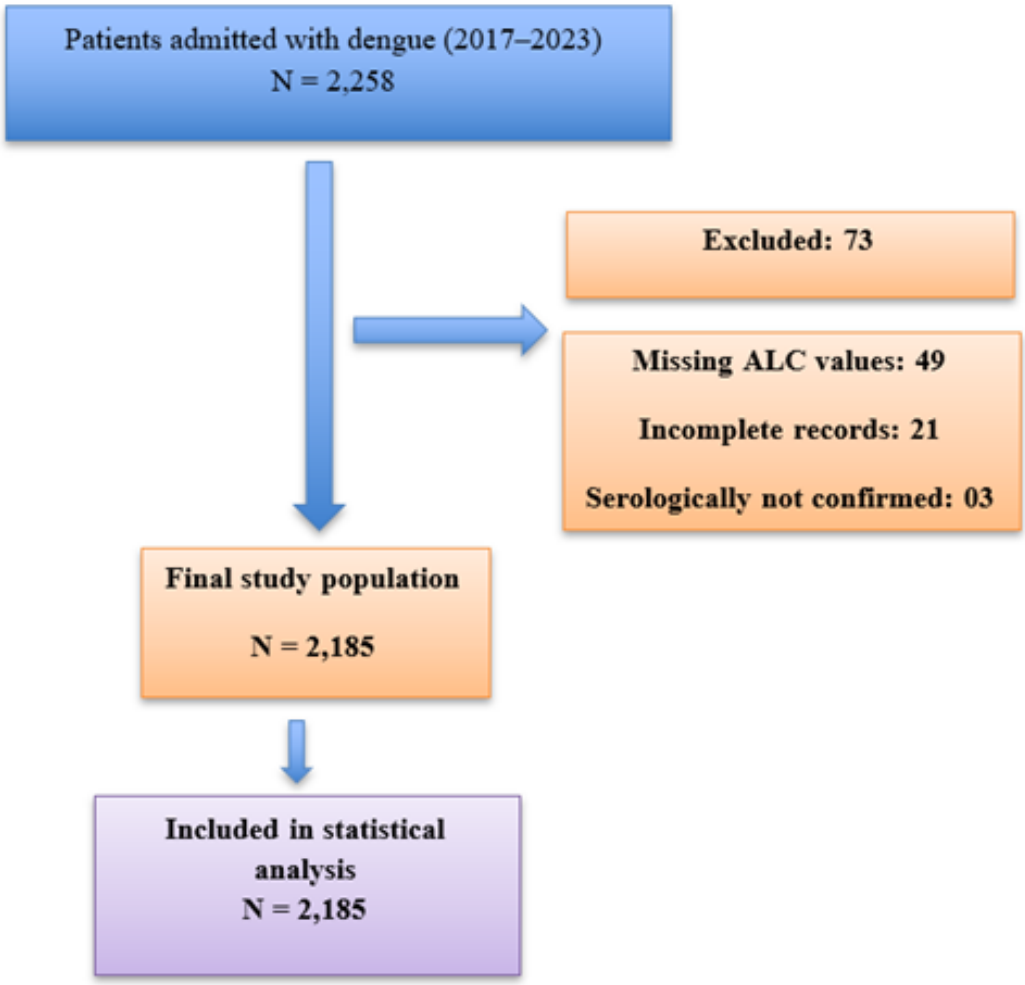

Fig. 1: Flowchart of Patient Selection.

Table 1: Socio demographic characteristics of the study population

Section	Variable	Number	%
Gender	Male	1050	48.1
	Female	1135	51.9
Age	Children (<15)	369	16.9
	Adolescents (15 to 24)	503	23
	Adults (25 to 44)	752	34.4
	Middle-aged (45 to 59)	470	21.5
	Elderly (≥ 60)	91	4.2
Insurance	Yes	1255	57.4
	No	930	42.6
Severity	Dengue without warning signs	1855	84.9
	Dengue with warning signs	255	11.7
	Severe dengue	75	3.4
Length of Stay	Less than 5 days	1795	82.2
	6 to 10 days	370	16.9
	More than 11 days	20	0.9

Financial characteristics of the study sample were demonstrated in table 2. Data were skewedly distributed. The median total hospital bill was LKR 127,600 (IQR: 91,072.00 – 177,100.00) for the median length of hospital stay for 5 days. Out of the total bill larger portions of the bill is contributed due to cost of room charges and other administrative activities (LKR 116,850; IQR: 80,050.00 – 159,225.00).

Table 2: Financial characteristics of study sample

Variable	Median (LKR)	IQR (25^{th} to 75^{th})
Cost of lab investigations	18,550.00	10,675.00 – 33,000.00
Cost of intravenous fluids and medication	17,879.16	9,654.29 – 27,684.07
Cost for the USS, X-rays, ECHO and ECG	4,812.50	1,300.00 – 12,425.00
Cost of room charges and other administrative activities	116,850.00	80,050.00 – 159,225.00
Total hospital bill	127,600.00	91,072.00 – 177,100.00

Table 3 shows the association between dengue severity and the hospital bill. There was a significant difference between dengue categories and the cost of

lab investigations, intravenous fluids and medication, Ultrasound scan(USS) ,X-rays ,ECHO and ECG, room charges and other administrative and total hospital bill.(Kruskal-Wallis test ; P<0.001). The highest expenditure was for the treatment of the severe dengue in comparison to other two groups.

Table 3: Association between dengue severity and hospital bill

Cost	**Dengue without warning signs**	**Dengue with warning signs**	**Severe dengue**	**Significance**[1]
Cost of lab investigations (Median) [LKR]	16,162.50	35,895.00	43,591.80	0.001***
Cost of intravenous fluids and medication (Median) [LKR]	17,154.24	25,752.79	41,141.81	0.01**
Cost for the USS, X-rays, ECHO and ECG (Median) [LKR]	3,996.00	18,005.00	57,057.75	0.001***
Cost of room charges and other administrative activities (Median) [LKR]	104,075.00	209,875.00	301,200.00	0.001***
Total hospital bill (Median) [LKR]	116,950.00	241,340.00	371,200.00	0.001***

[1] Kruskal-Wallis test; (* for p<0.05, ** for p<0.01, *** for p<0.001)

Table 4 shows the association between hospital cost and gender, age, availability of insurance and length of stay. Male patients had significantly higher costs for laboratory investigations, intravenous fluids and medications, ultrasound scans, X-rays, ECHO, and ECG ($p < 0.05$). However, differences in room charges and administrative costs were not statistically significant ($p = 0.21$). The older the age category, expenditure on lab investigations, intravenous flu-

ids and medication and Ultrasound scan ,X-rays ,ECHO and ECG had significantly higher costs patients had to bear (P<0.05). Patients with insurance had significantly higher bills compared to those without.(P<0.05). Patients who had a length of stay more than 5 days had significantly higher expenditure than those who were discharged early.

Table 4: Association between hospital cost and gender, age, availability of insurance and length of stay.

Variable	Cost of lab investigations (Median) [LKR]		Cost of intravenous fluids and medication (Median) [LKR]		Cost for USS, X-rays, ECHO and ECG (Median) [LKR]		Cost of room charges and other administrative activities (Median) [LKR]		Total hostpital bill (Median) [LKR]	
Gender										
Male	20,835.60	0.01**	21,817.42	0.01**	5,995.00	0.01**	119,712.50	0.21	131,900.00	0.01**
Female	15,481.20		17,431.24		4,099.40		111,900.00		122,250.00	
Age (Years)										
Less than 20	18,550.00	0.038*	17,781.31	0.001***	5,243.05	0.042*	116,950.00	0.116	128,000.00	0.367
21 to 40	18,550.00		19,498.01		5,243.05		113,737.50		128,000.00	
41 to 60	16,546.40		17,154.24		4,185.00		116,950.00		122,250.00	
Above 61	25,778.40		21,994.44		3,859.75		112,981.25		119,620.00	
Availability of Insurance Scheme										
Yes	22,130.55	0.01**	20,505.43	0.01**	5,274.80	0.01**	5,274.80	0.01**	127,500.00	0.01**
No	17,736.45		17,033.15		4,195.00		4,195.00		104,075.00	
Length of Hospital Stay										
Less than 5 days	15,262.95	0.001***	16,841.28	0.001***	4,099.40	0.001***	103,250.00	0.01**	112,220.00	0.01**
More than 5 days	35,895.00		35,830.20		16,596.25		209,875.00		127,600.00	

Note: * p<0.05, ** p<0.01, *** p<0.001.
*Mann–Whitney U test; **Kruskal–Wallis H test.

Table 5 shows the predictive factors for the total hospital bill (as a dependent variable) of the dengue patients. Severe dengue fever (B: 181,948.78; P<0.001), length of hospital stay more than 5 days (B: 102,635.67; P<0.001) and availability of insurance scheme (B: 17,644.8; P<0.001) are significant predictors of the total hospital bill.

Table 5: Predictive factors of total hospital bill of dengue patients

Variable	B coefficient	95% CI	Significance[4]
Age	41.04	-87.78 – 169.88	0.532
Gender – Male[1]	3439.05	-691.29 – 7569.39	0.103
Severity of dengue – severe dengue[2]	181,948.78	169,523.39 – 194,374.18	0.001***
Length of hospital stay more than 5 days[3]	102,635.67	96,777.96 – 108,493.39	0.001***
Availability of insurance scheme	17,644.8	13,465.73 – 21,823.87	0.001***

[1]in comparison to female; [2]in comparison to dengue without warning signs and dengue with warning signs; [3]in comparison to length of stay less than 5 days; [4] Linear regression analysis. (* for p<0.05, ** for p<0.01, *** for p<0.001)

Predictive factors associated with length of hospital stay were demonstrated in table 6. Being a male patient (B:0.338 ; P<0.001), availability of insurance scheme(B:0.295 ; P<0.001) and severe dengue(B:4.876 ; P<0.001) were identified as significant predictors of length of hospital stay.

Table 6: Predictive factors associated with length of hospital stay

Variable	B coefficient	95% CI	Significance[1]
Gender – Male	0.338	0.209 – 0.467	0.001***
Availability of insurance scheme	0.295	0.164 – 0.426	0.001***
Severity of dengue – severe dengue	4.876	4.519 – 5.233	0.001***

[1]Linear regression analysis – stepwise method. (* for p<0.05, ** for p<0.01, *** for p<0.001)

Table 7a presents the association between atypical lymphocyte count (ALC) and dengue severity. Patients with ALC >0.5 × 10^3/μL were more frequently classified into the severe dengue category (236/428, 55.1%), whereas the majority of patients with ALC <0.5 × 10^3/μL were in the dengue without warning signs category (628/796, 79.1%). A chi-square test demonstrated a highly significant association between ALC category and dengue severity ($\chi^2(2) = 605.68$, $p < 0.001$).

Table 7b shows the relationship between ALC and clinical/economic outcomes. In both ALC groups, the Kruskal–Wallis H test indicated significant

differences in median length of stay and hospital costs across the three severity categories ($p < 0.001$). Furthermore, Mann–Whitney U tests revealed that patients with ALC $>0.5 \times 10^3/\mu L$ had significantly longer hospital stays and higher bills than those with ALC $<0.5 \times 10^3/\mu L$ within each severity group (all $p < 0.001$). These findings confirm the utility of ALC as an early prognostic marker for both disease severity and healthcare burden.

Table 7a: Association between ALC and Dengue Severity

ALC Category	**Without warning signs (N)**	**With warning signs (N)**	**Severe dengue (N)**	**Significance[1]**
ALC > 0.5 × 10^3 / μL	48	144	236	<0.001***
ALC < 0.5 × 10^3 / μL	628	140	28	

[1]Chi-square test: $\chi^2(2) = 605.68$, $p < 0.001$

Table 7b: Association between ALC and Length of Stay / Hospital Bill

ALC Group	**Category**	**Median length of stay (days)**	**Median hospital bill (LKR)**	**Significant[1]**
ALC > 0.5 × 10^3 / μL	Dengue without warning signs	5.5	132,000	<0.001***
	Dengue with warning signs	7	232,000	
	Severe dengue	9	324,000	
ALC < 0.5 × 10^3 / μL	Dengue without warning signs	4	116,000	<0.001***
	Dengue with warning signs	6	166,000	
	Severe dengue	7	201,000	

[1]Kruskal–Wallis H test; (* for p<0.05, ** for p<0.01, *** for p<0.001)

Figure 2 shows the On admission (day 3 following fever) AL count more than 0.5 $[10^3]$ as a predictive factor for patient's hospital stay more than 5days and total hospital bill more than LKR 132000. According to ROC curve analysis patients who had AL count more than 0.5 $[10^3]$ on admission there was 94% sensitivity and 78.4% specificity for a hospital stay lasting more than 5 days. Furthermore if on admission AL count more than 0.5 $[10^3]$ there was a 95.8% sensitivity and 72.4% specificity that hospital total bill will be more than LKR 132,000. The thresholds for hospitalization >5 days and hospital bill >LKR 132,000 were chosen as they corresponded approximately to the upper quartile (75th percentile) of our dataset, thereby identifying patients at highest risk of prolonged stays and elevated costs. While ROC analysis demonstrated high sensitivity (94.4–95.8%), specificity was lower (72.4–78.4%), indicating the possibility of false positives. (Table 8)

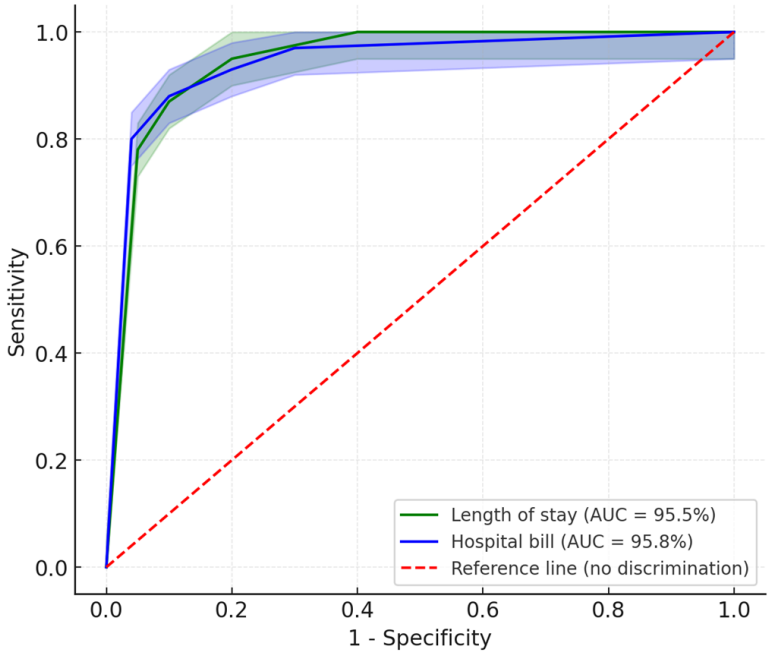

Fig. 2: ROC curve showing predictive value of ALC > 0.5 × 10³/μL for hospital stay > 5 days and total bill > LKR 132,000. Curves include 95% confidence intervals and the diagonal reference line (line of no discrimination).

4 Discussion

The main objective of this study is to evaluate the economic burden of dengue fever in the private sector health care system in a selected sample of patients in Sri Lanka and find out ALC as an early predictor to minimize the financial cost of the patient. According to our study female patients were dominant

Table 8: Sensitivity and specificity of the predictive value of ALC >0.5 × $10^3/\mu L$ for hospital stay >5 days and total bill >LKR 132,000

Variable	AUC [%] (95% CI)	Sensitivity	Specificity
Length of hospital stay more than 5 days	95.5 (91.4–97.2)	94.4	78.4
Total hospital bill more than LKR 132,000	95.8 (92.2–96.9)	94.5	72.4

and the most prominent age category was 21 to 30 years. Furthermore, most of the patients do not have health insurance and need to bear the cost out of pocket during the hospital admission. It was 42.6% in our study sample. Studies which were carried out in south East Asia had reported that female patients were predominantly diagnosed with dengue fever (Murugananthan et al., 2012; Shrestha et al., 2022; Urmi et al., 2023). Based on a study which was conducted in Bangladesh with a sample size of 302 hospitalized confirmed dengue patients, it was summarized that the households out-of-pocket cost contributed to a larger portion of the total costs of illness (66%) while the cost burden was significantly higher for the poorest households than the richest quintile.(Sarker et al., 2023). This clearly demonstrates that out-of-pocket expenditure constitutes a significant economic burden in South Asian countries due to dengue fever.

According to our study, the total hospital bill for severe dengue, dengue with warning signs, and dengue without warning signs was LKR 371,200 (USD 1150.75), LKR 241,340 (USD 748.18) and LKR 116,950(USD 362.55) respectively. [Current USD to LKR conversion rate taken as LKR 322.57).Study conducted in India summarized that the median and interquartile range (IQR) direct costs for pediatric dengue without warning signs, dengue with warning signs, and severe dengue were 179.80 (IQR 85.51–428.51) USD, 145.06 (IQR 90.89–321.86) USD, and 933.51 (IQR 400.50–1117.43) USD, respectively. The median and IQR direct costs for adult dengue without warning signs, dengue with warning signs, and severe dengue were 312.75 (IQR 174.55–531.03) USD, 287.22 (IQR 210.96–389.34) USD, and 720.39 (IQR 389.23–1035.51) USD, respectively (Panmei et al., 2019).Furthermore study done Bangladesh shows that the average cost to society for a person with a dengue episode was US$ 479.02. This amount ranged between US$ 341.67 and US$ 567.12 for those patients who were treated at public and private hospitals, respectively (Sarker et al., 2023). The study conducted in government sector expenditure on dengue management care in Sri Lanka show that the average costs per hospitalization ranged between US$216–609 for pediatric cases and between US$196–866 for adult cases according to disease severity and treatment setting (Thalagala et al., 2016). The difference between the government and private sector is mainly due to higher overhead charges due to different taxes which are imposed to the private health sector in comparison to the state.

Our analysis demonstrates that room and administrative charges constitute the bulk of hospital expenditure. Importantly, adjusting for inflation across the 2017–2023 study period increased the accuracy of cost estimates and avoided misleading currency conversions. When applying an ALC-guided triage strategy, early discharge of low-risk patients (ALC $<0.5\times10^3/\mu L$) could potentially reduce mean hospitalization costs by an estimated 12–15%. Although a full cost-effectiveness model incorporating quality-adjusted life years (QALYs) was beyond the scope of this dataset, our scenario analysis suggests ALC-guided care may offer substantial savings, particularly for uninsured patients. Although our analysis estimated potential reductions in hospitalization costs, a cost-utility analysis incorporating quality-adjusted life years (QALYs) was not feasible due to the nature of available data. Prospective studies incorporating both clinical outcomes and patient-reported quality of life will be necessary to fully evaluate the cost-effectiveness of ALC-guided triage.

According to our study the predictive factors for the total hospital bill (as a dependent variable) of the dengue patients which were identified as severe dengue fever (B: 181,948.78; P<0.001), length of hospital stay more than 5 days (B: 102,635.67; P<0.001) and availability of insurance scheme (B: 17,644.8; P<0.001). A study conducted in China shows that the mean of the Length of Stay (LOS) and male dengue patients had significantly higher cost of dengue than female. (Zhang et al., 2017)

A unique finding of our study is the assessment of ALC and its predictive ability for hospital stay and total hospital cost for patients diagnosed with dengue. This has not been discussed previously in literature. However ALC and its discriminating power of the severity of dengue fever has been discussed in previous literature. A study conducted in Sri Lanka shows that severe dengue has a significantly higher AL % compared to dengue without warning signs. Furthermore they also highlighted that AL % at presentation may be predictive of severe DI (Clarice et al., 2019). Based on the literature to determine the association between on admission (day 3 following fever) ALC with dengue severity category, length of hospital stay and total hospital bill AL value more than 0.5 $[10^3]$ was selected (Abeysuriya et al., 2020). This study identified that ALC more than 0.5 $[10^3]$ on admission there was 94% sensitivity and 78.4% specificity for hospital stays lasting more than 5 days. Furthermore if on admission AL counts more than 0.5 $[10^3]$ there was 95.8% sensitivity and 72.4% specificity that hospital total bill will be more than SRL 132,000. This was a novel finding. It needs more study to generalize the study findings.

The biological plausibility of ALC as a prognostic marker is supported by its role as an indicator of activated T-lymphocytes and immunoblasts during viral infections. Elevated ALC may reflect immune hyperactivation and cytokine release, both of which contribute to plasma leakage and severe dengue manifestations. Importantly, ALC is measured on day 3 of fever, which corresponds to the transition into the critical phase of dengue, when warning signs typically appear. Therefore, while not an 'early' marker in the strictest sense,

ALC may still be clinically valuable for early risk stratification at the time of hospital admission.

When compared with established markers such as platelet count, hematocrit changes, and WHO clinical warning signs, ALC offers the advantage of being an objective, automated parameter included in routine full blood counts. Previous studies have demonstrated that ALC correlates with thrombocytopenia and disease severity (Clarice et al., 2019; Abeysuriya et al., 2020). Our findings suggest that ALC can complement, rather than replace, existing predictors, contributing to a multi-parametric approach to dengue risk assessment.

This study has several limitations. First, it was conducted at a single private tertiary care hospital, and therefore, the results may not reflect the economic and clinical burden in government hospitals or rural healthcare centers. The higher proportion of patients with health insurance (57.4%) compared to national averages suggests a potential socioeconomic selection bias. Second, no comparison was made with other predictive biomarkers (e.g., platelet count, hematocrit, or WHO warning signs), which could provide a broader perspective on prognostic performance. Future multicenter studies including both private and public sector hospitals are warranted to improve the generalizability of these findings. Furthermore, this study did not demonstrate variation of cost according to genetic type of dengue. This is mainly due to the unavailability of facilities to differentiate genotype of infections in our study setting. Another limitation was the inability to account for potential confounding factors such as co-morbidities and seasonal variations, which may influence both atypical lymphocyte count and dengue severity. Although age was included in regression models, other clinical parameters could not be controlled for due to data unavailability. These unmeasured confounders may partly explain the observed associations. We were unable to perform a fully adjusted multivariate analysis due to the absence of information on co-morbidities and seasonal trends. This limitation should be considered when interpreting the associations observed.

In addition, certain methodological constraints should be noted. The thresholds used in the ROC analysis (>LKR 132,000 for hospital bill and >5 days for hospital stay) were based on upper quartile values of our dataset rather than externally validated clinical or economic benchmarks, which may limit their generalizability. Although the ROC analysis demonstrated very high sensitivity (94.4–95.8%), the specificity was more modest (72–78%), implying a potential for false positives and unnecessary patient monitoring. Patients with missing atypical lymphocyte count (ALC) values were excluded from analysis, which could introduce selection bias. Finally, while our scenario analysis suggested possible cost savings with ALC-guided triage, a full cost-effectiveness model incorporating quality-adjusted life years (QALYs) was beyond the scope of this dataset. We did not perform a formal sensitivity analysis for alternative cost thresholds; therefore, our findings are most applicable to the upper-quartile definition of high-cost care.

Sample size considerations for prospective validation.

Our findings require prospective, multicentre validation. Using precision-based calculations to estimate diagnostic accuracy with a ±5% margin of error at 95% confidence, we estimate that validating the length-of-stay endpoint (>5 days; observed sensitivity 94.4% and specificity 78.4%) would require approximately $n \approx 460$ patients in total (at least ≈ 82 prolonged-stay cases, assuming a 17.8% prevalence). For the high-cost endpoint (>LKR 132,000; observed sensitivity 95.8% and specificity 72.4%), assuming a 25% prevalence of high-cost cases, approximately $n \approx 410$ patients would be required (≥62 high-cost cases). These targets ensure ±5% precision for the corresponding sensitivity/specificity estimates and can guide future validation studies.

5 Conclusion

Out of pocket expenditure was higher in dengue fever. Severity of dengue and length of hospital stay were major contributing factors to the hospital bill. On-admission ALC can be used as a predictive tool to estimate both hospitals stay duration and total costs. Early discharge of patients with low ALC will reduce the financial burden.

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