Clinical Profile of Patients with Dengue: A One-year Retrospective Study at a Tertiary Care Center

Bir Üçüncü Basamak Sağlık Merkezinde Dang Hummalı Hastaların Klinik Profili: Bir Yıllık Retrospektif Çalışma

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Abstract

Introduction: Dengue is an acute viral illness caused by the Flaviviridae RNA virus and spread by the Aedes mosquito. Being a tropical illness, knowledge of its demographic and clinical profiles and seasonal incidence can aid in the management and control of the disease. Additionally, it is important to know the relationship between thrombocytopenia, leukopenia, transaminitis, and the severity of dengue and its mortality and morbidity. It is aimed to assess the clinical profile of patients with dengue at a tertiary care center.

Materials and Methods: A retrospective observational study was conducted at a tertiary care hospital located in South India. The medical records of patients admitted between January 2022 to December 2022 were reviewed. A total of 582 patients were screened, and 539 patients with a definite diagnosis of dengue were selected based on the inclusion and exclusion criteria. We obtain data on the demographic and clinical profile of dengue, seasonal variation in the incidence of dengue, degree of thrombocytopenia, transaminitis, albumin/globulin (A/G) ratio and number of days in hospital. All the analyses were performed using Microsoft Excel 2021. The continuous variables are presented as means, standard deviations, and minimum and maximum values. The categorical variables are presented as frequencies and percentages.

Results: The present study included 539 participants with a mean age of 30.23±13.81 years. Most participants (80.52%) suffered from dengue without warning signs. The incidence of dengue was higher during winter (60.11%) than during the other seasons. Most participants suffering from dengue without warning signs had severe thrombocytopenia (49.35%), leukopenia (46.20%) and transaminitis severity of Grade 1 (35.44%) based on serum glutamic oxaloacetic transaminase levels and Grade 0 (39.89%) based on serum glutamic pyruvic transaminase levels. Furthermore, most of these patients had a normal A/G ratio (63.64%) and moderate morbidity (69.76%).

Conclusion: Dengue without warning signs was the most common type of dengue seen. These participants had varying degrees of thrombocytopenia, leukopenia, and transaminitis, moderate morbidity, and low mortality. The present study is the first of its kind to associate the type of dengue and different hematological conditions with the morbidity and mortality of patients with dengue which helps in early identification of types of dengue and effective management.

Keywords: Dengue, thrombocytopenia, leukopenia, morbidity, mortality

Öz

Giriş: Dang humması, Flaviviridae ailesinden bir RNA virüsünün neden olduğu ve Aedes sivrisinekleri ile taşınan akut viral bir hastalıktır. Tropikal bir hastalık olduğundan, demografik ve klinik profilleri ile mevsimsel görülme sıklığının bilinmesi hastalığın yönetimi ve kontrolüne yardımcı olabilir. Ayrıca trombositopeni, lökopeni ve transaminit (karaciğer enzim yüksekliği) ile dang hummasının ciddiyeti, mortalitesi ve morbiditesi arasındaki ilişkiyi bilmek önemlidir. Üçüncü basamak bir sağlık merkezinde dang humması olan hastaların klinik profillerinin değerlendirilmesi amaçlanmıştır.

Gereç ve Yöntem: Güney Hindistan'da bulunan üçüncü basamak bir hastanede retrospektif gözlemsel bir çalışma yürütüldü. Ocak 2022 ile Aralık 2022 arasında başvuran hastaların medikal kayıtları incelendi. Toplam 582 hasta tarandı ve dahil etme ve dışlama kriterlerine göre kesin dang humması tanısı alan 539 hasta seçildi. Dang hummasının demografik ve klinik profili, dang humması görülme sıklığındaki mevsimsel değişim,

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Öz

trombositopeni derecesi, transaminit derecesi, albümin/globulin (A/G) oranı ve hastanede yatılan gün sayısı verileri toplandı. Tüm analizler Microsoft Excel 2021 kullanılarak gerçekleştirildi. Sürekli değişkenler ortalama, standart sapma, minimum ve maksimum değerler olarak sunuldu. Kategorik değişkenler frekans ve yüzde olarak sunuldu.

Bulgular: Bu çalışmaya yaş ortalaması 30,23±13,81 olan 539 katılımcı dahil edildi. Katılımcıların çoğu (%80,52) herhangi bir uyarı belirtisi göstermeden dang hummasından muzdaripti. Dang insidansı kış mevsiminde diğer sezonlardan daha yüksekti (%60,11). Uyarıcı belirti olmaksızın dang hummasından muzdarip olan katılımcılarda ciddi trombositopeni (%49,35), lökopeni (%46,20), serum glutamik oksaloasetik transaminaz seviyelerine göre 1.derece transaminit (%35,44) ve serum glutamik piruvik transaminaz seviyelerine göre 0 derece transaminit (%39,89) mevcuttu. Ayrıca bu hastaların çoğu normal A/G oranı (%63,64) ve orta düzeyde morbiditeye (%69,76) sahipti.

Sonuç: Uyarıcı belirtilerin olmadığı dang humması en yaygın dang humması türüydü. Bu hastalarda değişen derecelerde trombositopeni, lökopeni ve transaminit, orta derecede morbidite ve düşük mortalite tespit edildi. Bu çalışma, dang humması tipini ve farklı hematolojik özelliklerini, hastaların morbidite ve mortalitesi ile ilişkilendiren ve dang humması türlerinin erken tanımlanmasına ve etkili bir şekilde yönetimine yardımcı olan ilk çalışmadır.

Anahtar Kelimeler: Dang, trombositopeni, lökopeni, morbidite, mortalite

Introduction

Dengue is a vector-borne disease whose incidence has been increasing alarmingly in recent decades. Dengue is underreported as most cases are mild, self-limiting, and asymptomatic[1].The dengue virus reportedly infects approximately 390 million people annually with 96 million showing clinical symptoms[2]. Approximately half of the global population residing in tropical and sub-tropical climate regions are at a risk of developing dengue[3]. Furthermore, the number of dengue cases reported in Southeast Asia has increased over the last decade[2].

Dengue is classified into three categories. The first type presents initially with the main symptoms: abrupt onset of high-grade fever (39 °C-40 °C), severe headache, retro-orbital pain, myalgia, and arthralgia. These symptoms usually subside after the third day of their onset and are categorized as dengue without warning signs[4].

After defervescence, this disease may progress to the second category, dengue with warning signs, which presents as severe and continuous abdominal pain, pleural and/or pericardial effusion, persistent vomiting, ascites, mucosal bleeding, postural hypotension, hepatomegaly, irritability, lethargy and a progressive increase in hematocrit. If these manifestations are not investigated, the disease can progress to the most dangerous category, severe dengue. This stage results in a range of outcomes including shock, hemorrhage, organ dysfunction, and even death[4].

Dengue is definitively diagnosed via serology and a viral antigen detection test[4]. Furthermore, knowledge of the clinical signs and symptoms of dengue is required to reduce the disease-associated morbidity and mortality by ensuring that patients are screened and definitively diagnosed using laboratory tests as soon as possible. Studies regarding the association between various hematological parameters and types of dengue and their outcome were lacking hence we conducted a retrospective study over a period of one year to ascertain the clinical profile of dengue. We aimed to obtain data on the demographic and clinical profile of dengue, seasonal variation in the incidence of dengue, degree of thrombocytopenia, transaminitis and its relation with mortality and morbidity (assessed by the number of days in hospital), and the severity of dengue (World Health Organization classification) and its relation with the degree of thrombocytopenia, leukopenia, transaminitis, and albumin-globulin (A/G) ratio.

Materials and Methods

A retrospective observational study was conducted at a tertiary healthcare center in South India. The study was approved by the Institutional Human Ethics Committee PSG Institute of Medical Sciences and Research (PSG/IHEC/2023/Appr/Exp/069, date: 13.02.2023). Since this was a case record based retrospective study participants consent was not required The study included all patients admitted to the healthcare center between January 2022 and December 2022, and convenience sampling was followed. A total of 582 patients were screened, and 539 patients with a definite diagnosis of dengue were selected based on the inclusion and exclusion criteria. The medical records of 582 patients who were diagnosed with dengue and aged >12 years were reviewed. Patients with comorbid illnesses such as connective tissue disorder, systemic lupus erythematosus (SLE), and chronic decompensated liver disease, and those with acute hepatitis A or B and scrub typhus infections were excluded. Finally, 539 patients were included in the study.

Participants were included in the study if they were diagnosed using dengue NS1 or IgM/IgG enzyme-linked immunosorbent assay or dengue IgM chemiluminescent immuno assay, were aged >12 years, and were admitted within the study period.

The platelet count was assessed and the degree of thrombocytopenia was classified as follows: normal, ≥150,000/µl; mild, 100,001 to-150,000/µl; moderate, 50,001 to 100,000/µl; and severe, ≤50,000/µl. The absolute neutrophil counts (ANCs) were classified as follows: severe, <500/µl; moderate, 501 to 1,000/µl; mild, 1,001 to 1,500/µl; and normal >1,500/µl. The total white blood cell (WBC) count was assessed; total count of <4,000 mm³ was considered as leukopenia, and total count of >4,000 mm³ was considered normal. Morbidity was classified based on the duration of hospital stay as follows: mild, ≤2 days; moderate, 3-5 days; and severe, ≥6 days. The A/G ratio was used to assess liver injury; an A/G ratio of >1 was considered normal, and an A/G <1 was considered abnormal. The severity of transaminitis based on serum glutamic oxaloacetic transaminase (SGOT) (or AST) was graded as follows: Grade 0, 15 to 41 IU/l; Grade 1, 42 to 122 IU/l, Grade 2, 123 to 205 IU/l, Grade 3, 206 to 820 IU/l, and Grade 4, ≥820 IU/l. The severity of transaminitis based on serum serum glutamic pyruvic transaminase (SGPT) (or ALT) levels was graded as follows: Grade 0, 17 to 63 IU/l; Grade 1, 64 to 188 IU/l; Grade 2, 189 to 315 IU/l; Grade 3, 316 to 1,260 IU/l; Grade 4, ≥1,260 IU/l.

Statistical Analysis

All the analyses were performed using Microsoft Excel 2021 (Office 365; Microsoft Corporation Washington, USA). The continuous variables are presented as means, standard deviations, and minimum and maximum values. The categorical variables are presented as frequencies and percentages. The results have been elaborated in tables.

Results

Male participants were on a higher proportion (53.80%) than that of female participants and dengue without warning signs was the most common presentation (80.52%) (Table 1). Most participants had severe thrombocytopenia (63.45%), normal ANC levels (62.71%), and leukopenia (56.59%). Most patients has normal A/G ratios (76.07%). The highest dengue incidence was reported in the winter (60.11%). The predominant transaminitis severity grading based on SGOT (AST) and SGPT (ALT) levels was Grade 1 (42.49%) and Grade 0 (47.31%), respectively. The morbidity status and mortality rate of most patients was moderate (85.16%) and 0.37%, respectively.

The present study included 539 participants with a mean age of 30.23±13.81 years (Table 2). The mean total WBC count of all participants was 4315.96±2511.48/µl, and the mean ANC was 2212.06±1599.42/µl. The mean duration of hospital stay was 3.91±1.25 days.

Most of participants (49.35%) suffering from dengue without warning signs had severe thrombocytopenia or leukopenia (46.20%) (Table 3). Most of the participants suffering from dengue without warning signs had a transaminitis severity

Table 1. Demographic and clinical profile of the patients with dengue

Variable	Sub-category	n	%
Sex	Male	290	53.80
	Female	249	46.20
Dengue classification	Dengue with warning signs	82	15.21
	Dengue without warning signs	434	80.52
	Severe dengue	23	4.27
Degree of thrombocytopenia	Severe	342	63.45
	Moderate	134	24.86
	Mild	40	7.42
	Normal	23	4.27
ANC	Normal	338	62.71
	Mild	102	18.92
	Moderate	86	15.96
	Severe	13	2.41
Total count	Leukopenia	305	56.59
	Normal	234	43.41
A/G ratio*	Normal	410	76.07
	Abnormal	80	14.84
Seasonal variation of dengue incidence	Summer	47	8.72
	Winter	324	60.11
	Monsoon	168	31.17

Table 1. Continued

Variable	Sub-category	n	%
Transaminitis severity based on SGOT (AST) levels (IU/l)	Grade 0	57	10.58
	Grade 1	229	42.49
	Grade 2	120	22.26
	Grade 3	118	21.89
	Grade 4	15	2.78
Transaminitis severity based on SGPT (ALT) levels (IU/l)	Grade 0	255	47.31
	Grade 1	209	38.78
	Grade 2	46	8.53
	Grade 3	26	4.82
	Grade 4	3	0.56
Morbidity status	Mild	30	5.57
	Moderate	459	85.16
	Severe	50	9.28
Mortality	Yes	2	0.37
	No	537	99.63

*The total may not tally to 100% as data are missing.

n: Number of participants, %: Percentage of participants, SGOT: Serum glutamic oxaloacetic transaminase, SGPT: Serum glutamic pyruvic transaminase, ANC: Absolute neutrophil count, A/G: Albumin/globulin

Table 2. Mean and standard deviation of the demographic and hematological data

Variable	Mean	Standard deviation	Minimum value	Maximum value
Age (in years)	30.23	13.81	12	80
Total WBC count (count/microL)	4315.96	2511.48	1100	24800
ANC (count/microL)	2212.06	1599.42	200	15950
Platelet count (mm³)	50545.45	45110.6	3000	289000
SGOT (AST) (IU/l)	260.33	1638.65	11	37405
SGPT (ALT) (IU/l)	121.51	362.60	6.00	7613
Albumin	3.47	0.50	1.70	5.10
Globulin	2.89	0.42	1.50	4.70
A/G ratio	1.22	0.24	0.57	2.13
Duration of hospital stay (in days)	3.91	1.25	1	11

SGOT: Serum glutamic oxaloacetic transaminase, SGPT: Serum glutamic pyruvic transaminase, ANC: Absolute neutrophil count, A/G: Albumin/globulin, WBC: White blood cell

of Grade 1 (35.44%) based on the SGOT levels and Grade 0 (39.89%) based on the SGPT levels. Furthermore, most of these patients (63.64%) had a normal A/G ratio. Most participants (69.76%) suffering from dengue without warning signs had moderate morbidity.

Discussion

Globally, the health of people is going through a critical phase due to the increased incidence of vector-borne diseases among humans[5]. Dengue is the commonest arbovirus infection in the world and a major public health concern. The spectrum of this disease varies from a self-limiting course to life-threatening manifestations[6]. From 2017 to 2022, approximately 0.8 million dengue cases were reported in India[7].

The present study included 539 participants with a mean age of 30.23±13 years. This result was comparable to that of the study by Jisamerin et al.[1] (2021), in which most of the patients with dengue were aged 21-40 years. This result was also seen in other studies, such as those conducted by Mahmood et al.[8] (2021), Padyana et al.[9] (2019) and Khetan et al.[10] (2018)[11]. A review conducted by Badoni et al.[7] (2023) determined that patients aged 11-17 years reported the highest incidence of dengue in the year 2018-2019; this result is in contrast to the present study results.

The mean duration of hospital stay among the participants was 3.91±1.25 days. This result differed from that of a previous study where most patients with dengue (78.7%) stayed in the hospital for >6 days. This difference can be explained by the fact

Table 3. Severity of dengue and its relationship with the degree of thrombocytopenia, leukopenia, transaminitis, albumin/globulin ratio, and morbidity rate

Variable	Sub-category	Dengue without warning signs		Dengue with warning signs		Severe dengue	
		n	%	n	%	n	%
Degree of thrombocytopenia	Severe	266	49.35	56	10.39	20	3.71
	Moderate	114	21.15	18	3.34	2	0.37
	Mild	33	6.12	6	1.11	1	0.19
	Normal	21	3.90	2	0.37	0	0
Leukopenia	Yes	249	46.20	50	9.28	6	1.11
	No	185	34.32	32	5.94	17	3.15
Transaminitis severity based on the SGOT levels	Grade 0	53	9.83	4	0.74	0	0.00
	Grade 1	191	35.44	30	5.57	8	1.48
	Grade 2	99	18.37	17	3.15	4	0.74
	Grade 3	85	15.77	28	5.19	5	0.93
	Garde 4	6	1.11	3	0.56	6	1.11
Transaminitis severity based on the SGPT levels	Grade 0	215	39.89	35	6.49	5	0.93
	Grade 1	169	31.35	30	5.57	10	1.86
	Grade 2	33	6.12	11	2.04	2	0.37
	Grade 3	17	3.15	6	1.11	3	0.56
	Garde 4	0	0.00	0	0.00	3	0.56
Albumin/globulin ratio*	Normal	343	63.64	55	10.20	12	2.23
	Abnormal	59	10.95	13	2.41	8	1.48
Morbidity	Mild	28	5.19	2	0.37	0	0.00
	Moderate	376	69.76	68	12.62	15	2.78
	Severe	30	5.57	12	2.23	8	1.48

*The total may not tally to 100% as data are missing.

n: Number of participants, %: Percentage of participants, SGOT: Serum glutamic oxaloacetic transaminase, SGPT: Serum glutamic pyruvic transaminase

that the previous study included more patients suffering from dengue with warning signs (22.3%) than the present study did (15.21%)[1].

The proportion of male (53.80%) and female (46.20%) participants was almost equal in the present study, which is comparable with the results of some previous studies[1,12]. However, multiple other studies have reported that more males suffer from dengue than females[2,3,8,10,11,13]. Furthermore, a 5-year study conducted by Villalon et al.[14] (2021) at an elderly healthcare facility reported that more females than males suffered from dengue; this may indicate that females are more prone to developing a dengue infection at an advanced age than males.

Most participants (80.52%) included in the present study suffered from dengue without any warning signs. This contradicted the results of studies conducted by Jisamerin et al.[1] and Rafi et al.[3] that reported that 58% and 48.6% of the study participants suffered from dengue without warning signs. This result is reinforced by a study conducted by Tewari et al.[12] (2018).

Most study participants (63.45%) had severe thrombocytopenia. Additionally, most of the patients suffering from dengue without warning signs had severe thrombocytopenia. These results were similar to those reported by Mahmood et al.[8] (2021), who reported that most patients with dengue (73.2%) had severe thrombocytopenia. Another study conducted by Islam et al.[13] (2022) also reported that 57.95% of patients with dengue had platelet counts <50,000/μl. This result contradicted the results of previous studies, where 92.7% and 70.36% of patients with dengue developed moderate thrombocytopenia[1,5]. Vijay et al.[2] (2022) determined that 77% of patients with dengue have a platelet count of <100,000/μL, which differs from the present study results. Multiple studies have reported that thrombocytopenia is the most common hematological finding among patients with dengue[3,12,14-17]. A study by Agarwal et al.[18] (2018) also determined that a low platelet count is associated with severe dengue.

Most of the study participants had leukopenia (count <4,000/mm³). Furthermore, most of the participants suffering from dengue without warning signs had leukopenia. This result was

comparable to that of a previous study, in which the total WBC count was <4,000 mm³ in 51% of the patients with dengue[2]. Similar results were observed in other studies[3,8,13,14,17]. In contrast, one study reported that only 4% of the patients with dengue have leucopenia[1].

The incidence of dengue was higher during the winter than during the other seasonsin the present study. This result is in contrast with that of a 2-year study conducted by Badoni et al.[7] (2023), where most of the cases were seen during the post-monsoon season (September and October). In another study, the incidence of dengue was highest in October (79.51%)[5].

The severity of transaminitis was Grade 1 based on the SGOT (AST) levels (42% of patients) and Grade 0 based on the SGPT (ALT) levels (47% of patients). This was in contrast with results of a study conducted by Rafi et al.[3], where fewer patients with dengue had ALT >42 IU/l (12.5%) and AST >37 IU/l (5%). Prasad and Bhriguvanshi[19] (2019) reported increased AST and ALT levels among 87% and 80% of patients with dengue respectively, which is much higher than the incidence reported in the present study.

Most patients in the present study had moderate morbidity. The reduced morbidity may be attributable to the fact that participants with any kind of comorbidity affecting liver function or causing thrombocytopenia/other conditions were excluded.

The mortality rate in the present study was low (0.37%). This result is comparable to that of a 1-year study conducted by Singhal and Kothari[20] (2020), in which the mortality rate was 2.6%. Tewari et al.[12] also reported a mortality rate of 1% among patients with dengue. Padyana et al.[9] reported a mortality rate of 21.1%, which is significantly higher than that of the present study. This disparity can be attributed to the fact that most of the patients included in the previous study had comorbidities such as diabetes and hypertension.

Study Limitations

A limitation of the present study was that the study was conducted at a single healthcare center, which may not accurately reflect the incidence of dengue infections in different settings. Our study results indicate that the clinical profile of patients with dengue can aid in the screening of patients to definitively diagnose dengue and ensure early treatment to avoid the disease progression which is associated with higher morbidity and mortality rates. In future prospective studies including the degree of fall of platelet count, degree of transaminitis, its relation with day of illness and type of dengue are needed to further know about the progression of the disease.

Conclusion

The present study is the first of its kind to associate the type of dengue and different hematological conditions with the morbidity and mortality of patients with dengue. The study results indicate that most patients suffer from dengue without warning signs and develop thrombocytopenia and leukopenia. Furthermore, the mortality rate in the study was low. Our study emphasise the necessity for definite diagnosis of dengue and monitoring for thrombocytopenia and transaminitis in those patients to reduce the mortality.

Ethics

Authorship Contributions

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