



# Outcome of Patients Waitlisted for Deceased Donor Liver Transplantation During COVID-19 Pandemic: A Single-Center Experience

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**Background and aim:** COVID-19 pandemic has strained several healthcare resources across the world. While liver transplantation (LT) is the only curative therapy for patients with end-stage liver disease, we aimed to determine the clinical outcome of patients waitlisted for deceased donor liver transplantation (DDLT) during COVID-19 pandemic. **Methods:** A retrospective comparative observational study of adult patients waitlisted for DDLT from January 2019 to January 2022 at our liver unit (Dr Rela Institute and Medical Center, Chennai, Tamil Nadu, India) was carried out. Patient demographics, disease etiology, Model for End-Stage Liver Disease – Sodium (MELD-Na) score were calculated for all patients listed during the study period. Clinical event was defined as number of DDLT, death in the absence of transplant, and patients awaiting LT were compared. Statistical analysis was performed with SPSS V24.0. **Results:** In total, 310 patients were waitlisted for DDLT, of whom 148, 63, and 99 patients listed during 2019, 2020, and 2021 (till January 2022), respectively; 22 (53.6%), 10 (24.3%), and 9 (21.9%) patients underwent DDLT in the year 2019, 2020, and 2021 ( $P = 0.000$ ); 137 patients (44.19%) died on the DDLT waitlist of whom 41 (29.9%), 67 (48.9%), and 29 (21.1%) in the year 2019, 2020, and 2021 ( $P = 0.000$ ), respectively. Waitlist mortality was significantly higher during the COVID first wave. **Conclusion:** COVID-19 pandemic has significantly impacted patients waitlisted for DDLT in India. With limited access to healthcare facilities and decreased organ donation rates during the pandemic, there was a considerable reduction in the patients waitlisted for DDLT, lesser number of patients underwent DDLT, and higher waitlist mortality during the pandemic year. Efforts to improve organ donation in India should be strongly implemented. (J CLIN EXP HEPATOL 2023;13:601–607)

Since the declaration of Corona virus infectious disease (COVID-19) as “pandemic,” global healthcare has suffered a significant setback affecting billions of people.<sup>1,2</sup> India was badly affected by COVID-19 both in first and more so in the second wave leading to substantial depletion of healthcare resources.<sup>3</sup>

In the absence of definitive therapy, several measures have been implemented across various countries to reduce disease transmission including face mask, social distancing, and implementation of lockdown.<sup>4,5</sup> Although these measures provided an initial brief respite, subsequent surge in the number of cases has depleted healthcare re-

sources worldwide. The pandemic, its containment measures, and resurgence of disease waves may have caused collateral damage in non-COVID-19 patients worldwide including in India.<sup>6,7</sup>

Liver transplantation (LT) is the only therapeutic option for patients with end-stage liver disease. With the current pandemic, this surgery has been considered as Tier 3b by the Centre for Medicare and Medicaid (CMS) procedures recommending not to postpone high-acuity surgery such as trauma transplants and cardiac interventions.<sup>8</sup> However, many centers refrained from performing the LT midst of the pandemic because of change in local health care policies with inclination toward COVID-19 patients, reduced availability of healthcare workers for non-COVID patients; risk of COVID-19 to the donor, recipient, and healthcare workers; implementation of lockdown measures; and travel restrictions.<sup>9,10</sup>

Organ donation rates vary in different parts of the world. Spain has the highest organ donation rates with 50 per million population (PMP) as of 2019.<sup>11</sup> Organ donation rate in India is with 0.34 PMP with an improving trend.<sup>12</sup> Comparatively, the state of Tamil Nadu in south India excels better with 1.8 PMP, contributing to 50% of national organ donation pool.<sup>13</sup> Deceased donor liver

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**Abbreviations:** AKI: Acute kidney injury; COVID-19: Corona virus infectious disease; CTP score: Child–Turcotte–Pugh Score; DDLT: Deceased donor liver transplantation; HBV: Hepatitis B virus; HCC: Hepatocellular carcinoma; HCV: Hepatitis C virus; HE: Hepatic encephalopathy; LDLT: Living donor liver transplantation; MELD-Na: Model for End-Stage Liver Disease – Sodium; NASH: Nonalcoholic steatohepatitis

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transplantation (DDLT) is the only way forward for patients with end-stage liver disease in the absence of suitable family donor.

In parallel with organ donation rates, the practice of LT varies across continents. DDLT is the most common modality in the West, whereas living donor liver transplantation (LDLT) is widely accepted in Asia including India. Transplant programs in southern India provide both DDLT and LDLT services. We aimed to study the impact of COVID-19 pandemic in patients waitlisted for DDLT at our center.

## MATERIALS AND METHODS

A retrospective comparative observational study of patients waitlisted for DDLT at our liver unit (Dr Rela Institute and Medical Center, Chennai, Tamil Nadu, India), from January 2019 to January 2022. Patient demographics, etiology of liver disease, Child–Turcotte–Pugh (CTP) score, Model for End-Stage Liver Disease – Sodium (MELD–Na) score were calculated between the study period (2019, 2020, and 2021). Number of hospitalizations, clinical complications, mortality while awaiting transplantation, number of DDLT, and number of patients opted for LDLT (donor – a suitable family member) from the DDLT waitlist for the recipient in the DDLT waitlist were recorded. Clinical event was defined as any of DDLT, patients opting for LDLT, death in the absence of transplant, or patients awaiting LT until the end of the study period. In addition, clinical events were calculated during COVID first wave (April 1, 2020, to December 31, 2020), second wave (April 1, 2021, to December 31, 2021) and compared with similar time frame in the previous year (April 1, 2021, to December 31, 2021). The study included all adult patients (above 18 years) waitlisted for DDLT with end-stage liver disease or hepatocellular carcinoma (HCC). Patients who were

initially evaluated for LDLT and underwent the surgery as planned were excluded from the analysis as they do not impact DDLT waitlist. Similarly, acute liver failure and pediatric transplants were excluded from the study.

## STATISTICAL ANALYSIS

Data analysis was carried using SPSS Version 24.0. Descriptive statistical analysis was performed to identify frequency, percentage, mean, SD, and 95% CI for summarizing the data during the study period 2019, 2020, and 2021. Patients who underwent DDLT, those opted for LDLT from DDLT waitlist, mortality during waitlist, gender distribution, disease etiology were evaluated between three time periods. Events during the study period such as hospitalization, reason for admission, and death were compared using the Chi-square or Fisher's exact tests. Age, MELD–Na at listing, at 3 months, and at 6 months, CTP score, timing of clinical events (from listing to DDLT, LDLT, and death), and number of hospitalization episodes have been compared using the ANOVA or the Kruskal–Wallis test, when appropriate. A 95% significance level ( $P < 0.05$ ) was assumed for statistical analysis.

## RESULTS

After exclusion of patients who underwent elective planned LDLT ( $N = 388$ ) during the study period, we identified 310 patients waitlisted for DDLT, of whom 148, 63, and 99 patients listed during 2019, 2020, and 2021 (till January 2022), respectively.

Demographic details are outlined in Table-1. This showed a mean age  $52.37 \pm 11.95$ ,  $51.44 \pm 11.07$ , and  $53.58 \pm 9.49$  years ( $P = 0.468$ ), Male: Female 5.4:1, 4.3:1, and 3.7:1 for 2019, 2020, and 2021 patient cohort ( $P = 0.512$ ), respectively. Disease etiology showed

**Table 1 Demographics Details of Study Patients.**

Variables	Study Year			P value
	2019 n = 148	2020 n = 63	2021 n = 99	
Age – Mean (SD)	52.37 (11.95)	51.44 (11.07)	53.58 (9.49)	0.468
Male: Female	5.4:1	4.3:1	3.7:1	0.512
NASH (%)	82 (55.4%)	30 (47.6%)	57 (57.6%)	0.209
Alcohol	33 (22.3%)	19 (30.2%)	26 (26.3%)	
HBV	6 (4.1%)	5 (7.9%)	6 (6.1%)	
HCV	9 (6.1%)	1 (6.3%)	2 (2.0%)	
AIH	9 (6.1%)	4 (6.3%)	8 (8.1%)	
Miscellaneous	9 (6.1%)	4 (6.3%)	0 (0%)	
MELD–Na at LISTING – Mean (SD)	19.68 (6.0)	20.51 (6.7)	19.60 (7.3)	0.646
MELD at 3 months – Mean (SD)	19.06 (7.2)	21.68 (7.8)	21.35 (5.8)	0.177
MELD at 6 months – Mean (SD)	20.25 (7.4)	19.78 (11.4)	20.0 (4.4)	0.979
Child–Pugh score at listing – Mean (SD)	9.44 (2.38)	9.40 (2.29)	9.53 (2.61)	0.940

nonalcoholic steatohepatitis (NASH): 82 (55.4%), 30 (47.6%), and 57 (57.6%); alcohol: 33 (22.3%), 19 (30.224%), and 26 (26.3%); Hepatitis B: 6 (4.1%), 5 (7.9%), and 6 (6.1%); Hepatitis C: 9 (6.1%), 1 (6.3%), and 2 (2.0%); AIH: 9 (6.1%), 4 (6.3%), and 8 (8.1%) ( $P = 0.209$ ) in 2019, 2020, and 2021, respectively. Liver disease severity scores showed MELD-Na  $19.68 \pm 6.0$ ,  $20.51 \pm 6.7$ , and  $19.6 \pm 7.3$  ( $P = 0.646$ ) at listing;  $19.06 \pm 7.2$ ,  $21.68 \pm 7.8$ , and  $20.0 \pm 4.4$  ( $P = 0.177$ ) at 3 months;  $20.25 \pm 7.4$ ,  $19.78 \pm 11.4$ , and  $20.0 \pm 4.4$  (95%CI 16.31–23.6) ( $P = 0.979$ ) at 6 months for 2019, 2020, and 2021 study cohort, respectively.

## CLINICAL EVENTS

Clinical events during the study period are shown in Table-2. Overall, 41 (12.6%) (including 15 patients from 2018) patients underwent DDLT, with 22 (53.7%), 10 (24.4%), and 9 (21.9%) patients in the year 2019, 2020, and 2021 ( $P = 0.000$ ), respectively. Fifty-nine (19.0%) out of 310 patients listed for DDLT opted for LDLT of whom 25

(42.4%), 16 (27.1%), and 18 (30.5%) in 2019, 2020, and 2021 ( $P = 0.000$ ), respectively; 137 (44.19%) patients died on the DDLT waitlist of whom 41 (29.9%), 67 (48.9%), and 29 (21.2%) in the year 2019, 2020, and 2021 ( $P = 0.000$ ). At the end of the last follow-up (January 2022), 77 (24.8%) patients awaiting DDLT. Eleven patients improved medically and were delisted.

## Comparison of events during COVID waves

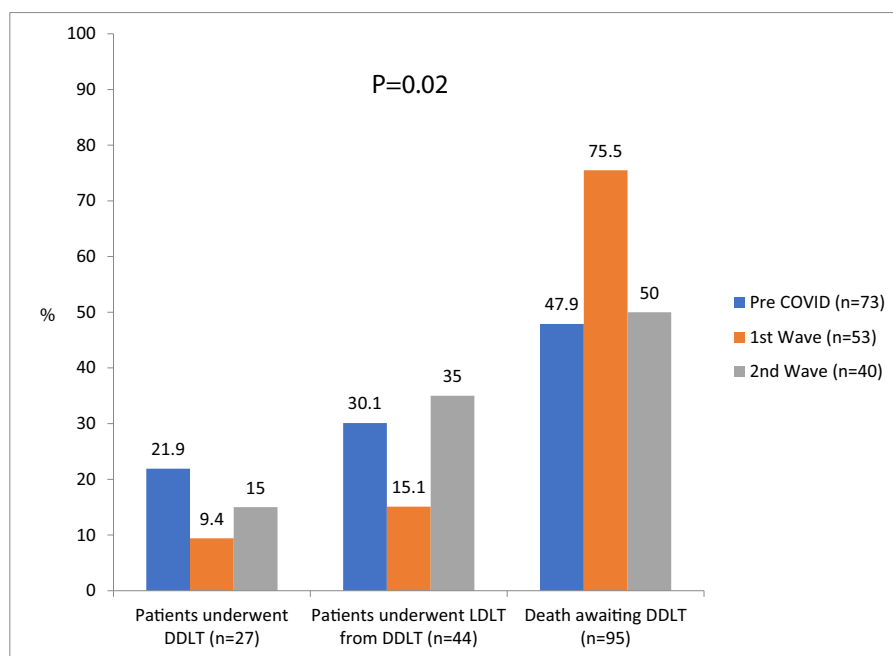
A comparative analysis of clinical outcomes from April 1 to December 31, 2019 (pre-COVID), 2020 (COVID first wave) and 2021 (COVID second wave) is illustrated in Figure 1. During the first wave, there was a trend toward a reduction in DDLT, DDLT patients opting LDLT, and a significant increase in waitlist mortality ( $P = 0.02$ ).

## Number of organ donations and waitlist mortality

A comparative analysis of organ donations in the state of Tamilnadu during the study period with number of

**Table 2** Illustrates Clinical Outcomes of Patients Waitlisted for DDLT During the Study Period.

DDLT waitlisted (N = 310)									
Total no of patients Listed for DDLT	2019		2020		2021				
No. patients	148		63		99				
Total	148/310 (47.7%)		63/310 (20.3%)		99/310 (31.9%)				
No. of DDLT (N = 26 + 15 (from the year 2018))									
Year of event	2019		2020		2021				
Total DDLT	22		10		9				
Year Listed	2018	2019	2018	2019	2020	2018	2019	2020	2021
No. Patients	12	10	2	7	1	1	1	3	4
Total	22/41 (53.7%)		10/41 (24.4%)		9/41 (21.9%)				
DDLT opted for LDLT (N = 59)									
Year of event	2019		2020		2021				
Year Listed	2019		2019		2020	2019		2020	2021
No. Patients	25		9		7	1		5	12
Total	25/59 (42.4%)		16/59 (27.1%)		18/59 (30.5%)				
Expired on the DDLT waitlist (N = 137)									
Year of event	2019		2020		2021				
Year Listed	2019		2019		2020	2019		2020	2021
No. Patients	41		36		31	2		6	21
Total	41/137 (29.9%)		67/137 (48.9%)		29/137 (21.2%)				
Awaiting DDLT (N = 77) till January 2022									
Year of event	2019		2020		2021				
Year Listed	2019		2020		2021				
No. Patients	11		6		60				
Total	11/77 (14.3%)		6/77 (7.8%)		60/77 (77.9%)				



**Figure 1** Comparison of clinical outcomes of patients waitlisted for DDLT during the period before COVID, first, and second wave.

DDLT at our center and waitlist mortality was carried out (Figure 2). The number of organ donations were 103, 45, and 58; the number DDLT were 22, 10, and 9; and the number of deaths on waitlist were 41, 67, and 29 patients, during 2019, 2020, and 2021, respectively. The ratio of organ donation to waitlist mortality was 2.5, 0.67, and 2.0 during the respective study years.

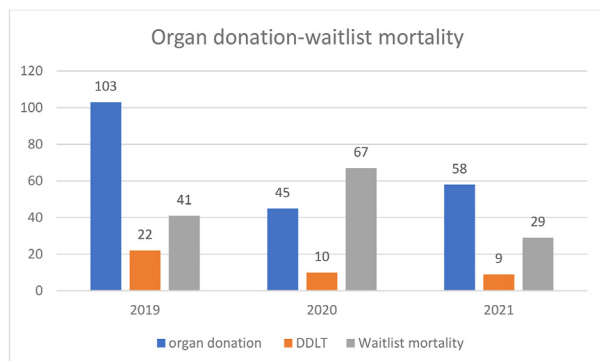
### TIMING OF CLINICAL EVENTS

Timing (in days) of clinical event from listing was calculated. There was no difference from listing to DDLT 224.38 (95%CI 144.7–304.1), 92.25 (95% CI 29.9–154.6), 252.8 (95%CI 203.2–302.4) ( $P = 0.182$ ), DDLT patients opting LDLT 182.3 (95% CI 126.9–237.8), 203.67 (95%CI 108.8–298.5), 84.5 (95% CI 51.5–117.5) ( $P = 0.086$ ), between three

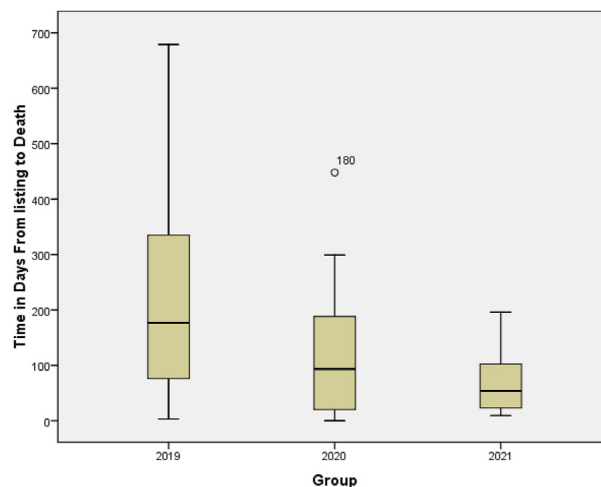
time periods, respectively. However, there was a statistical difference in time from listing to death 223.08 (95% CI 173.2–272.9), 118.27 (95% CI 66.8–169.7), and 74.2 days (95% CI 26.0–122.4) ( $P = 0.003$ ) (Figure 3).

### HOSPITALIZATION

Analysis of the study period showed no difference in the number of patients hospitalized 82 (55.4%), 34 (54%), and 61 (61.6%) between 2019, 2020, and 2021 cohort ( $P = 0.535$ ). Similarly, mean number of hospitalization episodes were 2.6 (95% CI 2.25–2.94), 2.29 (95%CI 1.86–2.73), and 2.28 (95% CI 1.92–2.64) with no significant difference between the study period ( $P = 0.363$ ).



**Figure 2** Comparison of organ donation, DDLT, and waitlist mortality during the study period.



**Figure 3** Time (in days) from listing to death.

The reason for hospital admission was kidney injury 6 (4.1%), 3 (4.8%), and 24 (24.2%) ( $P = 0.000$ ); hepatic encephalopathy 27 (18.2%), 14 (22.2%), and 5 (5.1%) ( $P = 0.003$ ); ascites 54 (36.5%), 23 (36.5%), and 29 (29.3%) ( $P = 0.460$ ); sepsis 22 (14.9%), 2 (3.2%), and 11 (11.1%) ( $P = 0.049$ ); gastrointestinal bleed 17 (11.5%), 9 (14.3%), and 10 (10.1%) ( $P = 0.718$ ); COVID 1 (0.7%), 4 (6.3%), and 1 (1.0%) ( $P = 0.017$ ); Transarterial chemo embolization (TACE) 4 (2.7%), 1 (1.6%), and 3 (3.0%) ( $P = 0.845$ ) for 2019, 2020, and 2021 study cohort, respectively.

## DISCUSSION

Our study clearly demonstrates the major impact of COVID-19 in patients waitlisted for DDLT. Perpetuated COVID-19 pandemic has caused collateral damage to patients with chronic diseases. Patients with long-standing clinical issues were unable to seek appropriate medical treatment particularly during the lockdown.<sup>14</sup> Most hospitals were unable to provide clinical service for non-COVID patients due to shunting of manpower and utility resources to manage COVID-19 patients.<sup>15</sup> In addition, the fear of risk of COVID-19 transmission has led to a significant compromise in patients requiring elective surgeries and other nonemergency services. In patients with chronic liver disease, services such as screening endoscopy, surveillance for HCC were refrained during the pandemic.<sup>16</sup> Further, international societies advocated postponement of elective surgeries including transplants amid the pandemic.<sup>17</sup>

Organ donation rates plummeted in most parts of the world during the pandemic, impacting patients awaiting solid organ transplantation and their programs.<sup>18</sup> Spain with one of the highest organ donations in the world reported a significant drop in deceased donors from 7.2 per day in 2019 to 1.2 per day in 2020, with corresponding reduction in the number of transplants dropping from 16.1 to 2.1 per day between January and March during pre-pandemic and pandemic year.<sup>19</sup> Italy was one of the worst affected countries in COVID's first wave, reported 25% decrease in deceased donors in the first 4 weeks.<sup>20</sup> Similarly, there was a 68% decline in organ transplantation in the UK between March and May 2020 compared to the previous year.<sup>21</sup> Likewise, USA observed a 25% reduction in donation nationally between February and April 2020 when compared to 2019.<sup>22</sup> Countries those enforced a complete lockdown noticed a severe drop in organ donations than those with partial lockdown.<sup>23</sup> Unlike the West, organ donation in India is still at its preliminary stage. Interestingly, within the country, the southern state of Tamil Nadu has better donation rates.<sup>24</sup> Unfortunately, donation rates dipped during the pandemic from 127 in 2019 to 57 organs in 2020.<sup>25</sup>

In patients requiring LT, several safety impediments were imposed during the pandemic. Liver Transplant Society of India guidelines on March 28, 2020, proposed restricting LT only for emergency indications such as acute liver failure and acute on chronic liver failure during the peak of the pandemic.<sup>26</sup> Similarly, Indian Society of Organ Transplantation guidelines dated March 3, 2020, recommended temporary suspension of living donor transplantation in view of risk to donor and recipient line with Ministry of health and Family Welfare's advisory committee.<sup>27</sup> However, LT being a life-saving procedure was selectively carried out in carefully selected high-risk patients with good outcomes.<sup>28</sup>

Implications of COVID-19 pandemic among patients waitlisted for DDLT in India are unclear. Our study showed a drastic drop in the number of patients waitlisted for DDLT (20.3%) during the pandemic. A SRTR database study from the USA demonstrated a transient reduction in the number of patients waitlisted and fewer (34%) DDLT between March and April 2020 but restored to normalcy after couple of months.<sup>29</sup> Unfortunately, such transformation is not reflected in India. This is probably related to suboptimal organ donation rates compounded by strict lockdown measures and limited accessibility to healthcare facilities during the current pandemic.

In our study, waitlist mortality for DDLT during COVID-19 pandemic was 75.5% in COVID 1st wave, which is higher than that reported from an Scientific Registry of Transplant Recipients (SRTR) database report (59%).<sup>30</sup> In addition, our study revealed significant shorter duration from listing to death during the pandemic. Fifty-nine (19%) waitlisted patients opted for LDLT, without which there may have been much higher waitlist mortality.

Our center has a unique opportunity and provision for both living related liver donor and cadaveric transplantation. In the absence of cadaveric LT, one would have expected to see an increase in waitlisted patients opting LDLT; interestingly, we did not encounter such a pattern during the pandemic. The reasons may be the COVID scare, strict lockdown measures, and in particular absence of suitable transportation facilities implemented during the lockdown. In addition to reduced organ donation rates, these factors could have contributed to the higher waitlist mortality encountered during the pandemic.

With a drastic reduction in organ donation rates during the pandemic as a result reduced road traffic accident, decreased the organ donation drive; a significantly higher proportion of patients are awaiting DDLT.<sup>31,32</sup>

The imitations of our study include single-center data, details such as Acute on Chronic Liver failure (ACLF) and nonliver related mortality were not obtainable as many events occurred in patients' native hospital.



Nonetheless, this is the only waitlist mortality study from India during COVID era.

COVID-19 pandemic and lockdown measure has impacted patients waitlisted for DDLT. With limited access to healthcare facilities and decreased organ donation rates during the pandemic, there was a considerable reduction in the patients waitlisted for DDLT, lesser number of patients underwent DDLT, and higher waitlist mortality during the pandemic year. Waitlist mortality may have been much higher in the absence of DDLT.

With partial resolution of COVID-19 waves, appropriate organ donation policies should be implemented and encouraged in countries like India to provide hope and life for these patients.

## CREDIT AUTHORSHIP CONTRIBUTION STATEMENT

**Dinesh Jothimani:** Conceptualization, data curation, analysis, writing, review.

**Evangeline Simon:** Data curation, statistical analysis.

**Swetha Palanichamy:** Data curation, statistical analysis, graphs.

**Sivakumar Murugesan:** Data curation.

**Hemalatha Ramachandran:** Statistical analysis.

**Vasudevan Sridhar:** Data analysis.

**Ilankumaran Kaliamoorthy:** Writing, critical appraisal.

**Akila Rajakumar:** Manuscript review.

**Gomathy Narasimhan:** Writing, review.

**Mohamed Rela:** Review, critical appraisal, overall supervision.

## CONFLICTS OF INTEREST

All authors have none to declare.

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None.

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