

Post-Discharge survival status and predictors of mortality among severely malnourished children <5 years of age admitted to Minia University Maternity and Children Hospital

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Abstract

Background: Though effective treatment programs for severely malnourished children are available, little is known about long-term outcomes and potential predictors of post-discharge mortality. The aim of this study was to assess the post-discharge survival status and predictors for post-discharge mortality in severely malnourished children admitted to Minia University Maternity and Children Hospital

Methods: A retrospective cohort study which included 135 children under five years of age who were admitted to the nutrition rehabilitation ward with severe acute malnutrition (SAM) during the period from January to December 2018. Data were collected from the inpatient's hospital records and the children's parents/guardians were interviewed using a detailed structured questionnaire that inquired about demographic and socioeconomic variables. The Cox proportional hazard model was used to assess the factors associated with the SAM's post-discharge mortality.

Results: A total of 135 children were enrolled into the study. Death rate during hospitalization was 9.6%. The cumulative probability of survival beyond eight weeks and at least for 24 weeks after discharge was 89.3% with a cumulative probability of post-discharge mortality of 10.7% and all deaths occurred within eight weeks after discharge. The main predictor for the SAM's post-discharge mortality was illiteracy of mothers; the multivariable HR (95%CI) was 7.10 (1.58-31.93; $p=0.01$).

Conclusions: Mothers' education and edema at admission are independent predictors for post-discharge mortality in under-five children with SAM. The identification of predictors for post-discharge mortality is an important preliminary step for interventions aiming to reduce morbidity and mortality following discharge.

Background

Malnutrition is one of the most common causes of morbidity and mortality among children all over the world. Of the 7.6 million annual deaths among children who are under 5 years of age [1], approximately 35% are due to nutrition-related factors and 4.4% of deaths have been shown to be specifically attributable to severe wasting [2]. A recent systematic review has indicated that the highest post-discharge mortality rates (3%–20%) in developing countries (mainly in Africa) were those for malnutrition and respiratory infections rather for other causes including anemia and malaria infection [3].

Sever acute malnutrition (SAM) is defined globally as a very low weight for length/height (WFL/WFH) below – 3 zscores of the median WHO growth standards, or less than 70% of the median National Center for Health Statistics standard or the presence of nutritional edema. In children aged 6–59 months, mid-upper arm circumference (MUAC) less than 11.5 cm is also an indicator of severe acute malnutrition [4]. Globally, 17 million children under 5 were affected by SAM [5]. In Egypt, there were no reports on accurate estimates for the prevalence of SAM. However, the anthropometric estimates from the Egypt Demography and Health Survey (EDHS) 2014 have indicated that 5.5% of the under-five children were underweight, 8.4% were wasted and 21.4% were stunted [6]. A cross-sectional study in Alexandria has found under-weight, stunting and wasting in 7.3%, 15% and 3.6% of the 1,217 preschool children aged 6-71 months [7]; while the estimated proportions among 400 under-five children in Fayoum were 23.2%, 18.5% and 19.3%, respectively [8].

Studying the treatment's outcomes of malnutrition and the potential predictors of mortality among severely malnourished children admitted to hospitals is a crucial step for enhancing the quality of care provided to malnourished children. However, there is a paucity of studies that reported mortality outcomes in severely malnourished children after being discharged from inpatient facilities [3,9,10], and none of the available studies was conducted in Egypt. Therefore, the objective of this study was to assess the post-discharge survival status and predictors for the post-discharge mortality in severely malnourished children admitted to Minia University Maternity and Children Hospital.

Methods

Study setting and population:

This retrospective cohort study was conducted at Minia University Maternity and Children Hospital, the only referral and teaching hospital in Minia governorate, Egypt. This hospital provides a wide range of health care services for urban and rural populations from near and far districts in Minia Governorate. The hospital has a Nutrition Rehabilitation Unit with a capacity of 60 beds and serves as a treatment center for children with malnutrition based on the standardized WHO protocol. The average number of examined malnourished children in this unit is around 40 patients per week and the unit annually serves, on average, 150 inpatient and 2000 outpatient malnourished children.

All children under 5 years of age who were admitted with SAM to the nutrition rehabilitation ward during the period from January to December 2018 were recruited for this study. SAM was diagnosed by the presence of severe wasting [z score for weight for height (WHZ) <-3.0 SD and/or the presence of nutritional edema [4]. All admitted children with SAM were managed according to the WHO protocol for management of SAM [4] and passed through initial stabilization phase (with the use of F75) and rehabilitation phase (F100). Whenever needed, other lines of treatment were also provided according to the WHO guidelines updates [4] after performing the required investigations such as stool analysis, complete blood picture, levels of C-reactive protein, blood glucose level, serum electrolytes (Na, K and ionized Ca), renal function tests and liver function tests. A daily check of weight gain during the treatment course was conducted and any complications appeared during the period of admission were managed.

Data collection procedure

The sources of data were the inpatient hospital records and checklists that were developed according to the standard treatment protocol for the management of SAM. Information collected were patient-related data, anthropometric measurements, comorbidities, type of SAM, treatment lines and others.

For the anthropometric measurements: in light clothing, young children <2 years old were weighed on a sensitive baby scale and children >2 years old were weighted on digital electronic scales. The weight records where they were taken to the nearest 0.1 kg. The length of children <2 years of age was measured in the recumbent position using wooden length board (Infantometer); while the standing height was measured for children aged 2 years or older by a stadiometer. The records were taken to the nearest 0.1 cm. Age and measurements of weight and height were plotted on the WHO and Z-score Growth Charts to determine the percentiles for each parameter. The Z-score is simply the difference between the observations' score (raw score) and the mean of

the total sample divided by the standard deviation of the total sample. A z-score of 0 represents the 50th percentile, a score of ± 1.0 falls on the 15th or 85th percentiles, respectively, while the score of ± 2 plots at the 3rd or 97th percentiles. These data were collected at the time of enrollment, during hospitalization, at discharge and at all follow-up appointments.

During hospital stay, children's parents/guardians were interviewed using a detailed structured questionnaire which inquired about the socioeconomic status and contact details (phone and address).

Fahmy and El-Sherbini's Social Classification Scale for assessing Egyptian socioeconomic status was used to classify the family socioeconomic status. This scale encompasses variables representing paternal education and work, housing conditions and family size and per-capita monthly income. Scores of 25-30 were considered a high social status, 20-<25 were regarded as middle social status, 15 to <20 indicated low social status while very low social status was defined at scores <15; details were given elsewhere [11].

Children were discharged from the hospital not on the basis of specific anthropometric measurement [4], but after achieving the following WHO criteria: a well and alert child with good appetite and without medical complications including resolving of edema [1,4].

Follow-up procedure:

All of the enrolled children who have survived hospitalization were requested to attend follow-up appointments for six months post-discharge as per routine follow-up schedule for the Nutrition Rehabilitation Unit in the hospital. Follow-ups were planned weekly for the first two weeks following discharge and biweekly thereafter. Routine procedures in each follow-up appointment included taking anthropometric measurements and vital signs, as well as assessing and managing of any current illness.

The main study outcome was to estimate the likelihood of a long-term post-treatment survival; six months post-discharge.

Statistical analysis:

Data entry and analyses were all done with IBM compatible computer using the SPSS for windows software version 22. Graphics were edited by the Excel Microsoft office 2013 software.

Quantitative data were presented by mean and standard deviation, while qualitative data were presented by frequency distribution. In the univariate analyses, the crosstabs command with the Fisher's exact test was used to compare between proportions and to impute the Hazard ratios (HRs) and 95% confidence Intervals (CIs) for dichotomous variables.

Children who started the follow-up plan and were not seen in subsequent appointments, with no knowledge of their death, were treated as censored cases at the time of their last follow-up appointment. Person-weeks of follow-up were calculated from time of hospital discharge (alive) to one of the denouements outcomes (death, lost to follow-up or end of the study, i.e complete 24 weeks of follow-up).

A Kaplan–Meier curve was plotted for the cumulative survival across follow-up appointments' time, and the multivariable-adjusted HRs; 95% CIs were calculated by the Cox proportional hazard model that included

variables which were significantly associated with the outcome in the univariate analysis. A statistically significant level was considered when a two sided p-value was less than 0.05.

We used the semiparametric Cox's regression model rather than typical parametric methods (such as Weibull, exponential, log-normal, and log-logistic models) because there was no evidence of violation of the proportional hazard assumption and we had no priori determination of a specific shape of the survival time, and believed that there was no strong effect or strong time trend in covariates or follow-up depending on covariates.

We ran a sensitivity analysis comparing the survival among those wasted ($WLZ < -3$) and those with edema.

Results

The age range of all admitted children within the specified period of the study ranged from 6 to 59 months. We excluded three children who have died within 6 hours of admission, and by revising their records they were of extreme WHZ (-5), height for age z scores (HAZ) of -6 or weight for age z scores (WAZ) of -6; however, we could not verify if these measurements were valid or errored. Thus, a total of 154 children were hospitalized with SAM; however, a total of 19 caregivers were unwilling to participate, leaving 135 children eligible for the study, with a response rate 87.7%. An informed consent was taken from the children's caregivers. During hospitalization, 13 (9.6%) children died and 122 (90.4%) were discharged alive with a follow-up plan. Parents of 18 discharged children refused to participate in the follow-up plan; leaving 104 children in the follow-up plan (Supplemental Figure I).

The mean age of those 135 children was 10.2 ± 8.6 months, and 49.6% of them were males, 60% were rural residents and 57% belonged to families with very low/low socioeconomic status. Out of 135 children, 58 (43%) had edema, with or without a WHZ of < -3 SD. The mean length of hospital stay was (15.47 ± 6.2) days, with the minimum and maximum lengths being six and 60 days, respectively. The majority (91.1 %) of the children had some co-morbidities/complications on admission in the form of dehydration (31.9 %), bronchopneumonia (23%) and sepsis (20.7%) (Table 1).

Out of total 122 children discharged alive, only 38 (31.1%) of them had achieved target weights of 85% weight for height at the time of discharge. The average weight gain was 10.4 g/kg/day (13g/kg/day for children with severe wasting and 7.3 g/kg/day for children with edematous malnutrition). These data were not shown in tables.

Out of 104 discharged children and their parents consented to participate in the follow-up study, 47 were last seen at one month after discharge, with no knowledge of outcomes; therefore, in the survival analyses, we treated them as censored at last time seen. In addition, seven have died and 50 children survived until at least the end of follow-up period of 24 weeks post-discharge (Supplemental Figure I).

The Kaplan–Meier curve for cumulative survival (Figure 1) and the survival table (Supplemental Table I) show that all deaths had happened soon within eight weeks after discharge; three at week four, two at week six and two at week eight. The cumulative probability of a child to survive up to four weeks after discharge was 96.4%, up to six weeks after discharge was 92.8%, and beyond eight weeks and at least for 24 weeks after discharge

was 89.3%. Accordingly, the post-discharge mortality rate was 3.6% within four weeks after discharge, 7.2% within six weeks after discharge, and 10.7% within eight to 24 weeks after discharge.

Comparing the survival among those wasted ($WLZ < -3$) versus those with edema showed a significant reduced likelihood for survival among edematous SAM; p value for the Log Rank test was 0.03 (Supplemental Figure II).

In univariate analyses for the factors associated with the post-discharge mortality/survival outcome among 104 children discharged alive with a follow-up plan, the mother's education and the absence of edema at admission were significantly associated with the post-discharge mortality/survival outcome (Table 2). Cox regression models included these two variables simultaneously showed HRs (95% CIs) for mortality in children of illiterate mothers versus that in children of educated mother of 7.10 (1.58-31.93; $p=0.01$) and in children with edematous malnutrition versus that in children with non-edematous malnutrition of 6.96 (0.84-57.85; $p=0.07$) (Table 3).

Discussion

In this follow-up study for children with SAM, the cumulative probability of a child to survive for \geq eight weeks and up to at least 24 weeks after discharge was 89.3%. Being a child of an educated mother was a significant predictor for a long-term survival in post-discharged SAM children admitted to and discharged from the Nutrition Rehabilitation Unit in Minia University Maternity and Children Hospital and completed six months of follow-up; while having a non-edematous malnutrition at admission tended to be associated with the long-term survival.

Over 70% of children hospitalized with SAM in our study were under one year of age. This confirms a high prevalence of SAM in younger children reported previously [12, 13]. The hospital care provided to children with SAM in Minia University Maternity and Children Hospital reached the SPHERE target of $<10\%$ mortality during hospitalization [14]. Thirteen out of 135 SAM cases, admitted to the hospital, died within one week of admission; the overall during hospitalization death rate was 9.6%. The most common causes of death were the malnutrition itself (eight cases), pneumonia (three cases) and sepsis (two cases).

The long-term; six months, post-discharge mortality rate in this study was 10.7%. All deaths had happened within eight weeks post-discharge, mostly due to pneumonia in six cases and one case was reported to die from severe uncontrolled bleeding per orifices. A study conducted among Bangladeshi under-five children reported 8.7% three-month post-discharge mortality rate following hospitalization with SAM and pneumonia [10]. Another study that included 393 Malawian children with SAM reported an 11% mortality rate within three months of hospital discharge [15]. The discrepancies in the reported mortality rates may be related to different study populations, study inclusion criteria or hospital discharge criteria. However, an important consideration is the timing of post-discharge deaths, most deaths had happened during the first several weeks of discharge, which indicates the importance of intervention during this period to help reduce the burden of deaths

The current study showed that illiteracy of mothers and associated edema at admission were found to be associated with post-discharge mortality in children with SAM admitted to the hospital. Mothers' education is one of the main determinants of under-five mortality [16]. In the current study, we found that maternal illiteracy was associated with 7-fold increased risk of post-discharge mortality. Our results are in line with the findings of

several studies [17-19]. Educated mothers versus illiterates are logically capable of coping with not only skills needed in post-discharge healthcare practices and disease treatment, but also those related to preventive care, such as child hygiene and nutrition, thus improving chances for the child survival [16-19].

Having edema with malnutrition at admission tended to be associated with the post-discharge mortality, though the association did not reach a level of significance in the multivariable adjusted analysis; $p=0.07$. This finding supports those from a study conducted by Kerac et al. [9] who have reported that Malawian children with edematous malnutrition were more likely to die than those without edema. On contrary, Jarso et al. [20] have found no mediating effects of edema on the survival status of discharged Ethiopian children.

Several studies have shown that the age and anthropometric measurements of the malnourished child at admission have significant roles in the post-discharge mortality of children with SAM [10,21-24]. However, we failed to find any effect of the children's age or anthropometric measurements at admission on the post-discharge mortality in our study. Girum et al. have indicated that the child's age but not anthropometric measurements was associated with the SAM's post-discharge mortality in 545 Ethiopian under-five children [25].

Strengths of this study include that data regarding the mortality predictors were collected at admission, before the discharge decision was made or the post-discharge outcomes were known, which reduced the potential for selection bias.

Limitations of the study:

The reliability of the recorded data could not be ascertained. Moreover, the proportion of children who were lost after one month of the follow up is huge; 45% of children assigned for the follow-up plan. This represents a major limitation for the generalizability of the study findings, and could have affected the power for significant inference and resulted in inflated confidence intervals of the estimated risk. However, we believe that this type of censoring was non-informative because there were no significant differences in children's characteristics such as age, sex, and anthropometric measurements at admission and at the latest follow-up appointment, nor in the family's socioeconomic levels, mother education and residence between children who completed the follow-up period and those who dropped out after one month of the follow-up (Supplemental Table II). Thus, a more or less similar post-discharge mortality rate; 10.7% might be expected among the censored cases. Yet, the confirmation of the study findings by further large-scale studies is needed.

Conclusion

This retrospective cohort study showed that, during hospitalization, the death rate of children with SAM admitted to the Nutrition Rehabilitation Unit in Minia University Maternity and Children Hospital reached the SPHERE target was <10%. Mothers' illiteracy was shown to be an independent predictor for, while the presence of edema at admission tended to be associated with, the post-discharge mortality. Furthermore, the long-term mortality rate was 10.7% within six months of hospital discharge, and all deaths happened soon after discharge. The results of our study indicate that the early post-discharge care represents a crucial integral extension of the hospital management for children with SAM. We recommend nutritional and hygiene educational programs for the caregivers of children with SAM during hospital admission and at time of

discharge with emphasizing on the need for continued access to health-care facilities and interventions to reduce the acquisition of new infections and to receive treatment for such conditions.

Abbreviations

SAM: Severe Acute Malnutrition

WFL/WFH: weight for length/height

Declarations

Ethics approval and consent to participate

Ethical approval was granted by the ethical committee of the Faculty of Medicine, Minia University. Prior to data collection, verbal informed consents were obtained from parents of all children after supplying comprehensive information about the nature of the study. Verbal consents were taken as considerable proportion were illiterate.

Consent to publish (Not applicable)

Availability of data and materials

The datasets generated and/or analyzed during the current study are not publicly available due [data contained from hospital records] but are available from the corresponding author on reasonable request.

Competing interests

The authors declare that they have no conflicts of interest relevant to the manuscript submitted to BMC Pediatrics.

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Authors' Contributions

GMB made substantial contributions to conception and design. ERG and ESE analyzed and interpreted the patient data, and were major contributors in writing the manuscript. GMB Collected the data and been involved in drafting the manuscript. All authors read and approved the final manuscript.

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Tables

Table 1: Demographic and admission characteristics for 135 severely malnourished children admitted to Minia University Hospital, January to December 2018

Frequency (%)	Variables
	Age (months)
98 (72.6)	6-12 m
31 (23.0)	12-24 m
6 (4.4)	>24 m
	Sex
67 (49.6)	Males
68 (50.4)	Females
	Residence
81 (60.0)	Rural
54 (40.0)	Urban
	Socioeconomic score¶
33 (24.4)	Very low social standard
44 (32.6)	Low social standard
48 (35.6)	Middle social standard
10 (7.4)	High social standard
	Admission anthropometric characteristics
77 (57)	WAZ < -3SD without edema
37 (27.4)	Edema with WAZ < -3SD
21 (15.6)	Edema without WAZ < -3SD
8 (5.9)	Stunting (HAZ < -2SD)
1 (0.7)	Severe stunting (HAZ < -3SD)
8 (5.9)	Wasting (WHZ < -2SD)
127 (94.1)	Severe wasting (WHZ < -3 SD)
15.47±6.2	Length of hospital stay (days)#
	Co-morbidity/complication at admission
43 (31.9)	Dehydration
31 (23.0)	Bronchopneumonia
28 (20.7)	Sepsis
21 (15.5)	Others

N.B. WAZ, weight for age z-score; HAZ, height for age z-score; WHZ, weight for height (z-score).

data presented as mean±SD.

¶ Fahmy and El-Sherbini's Social Classification Scale for assessing Egyptian socioeconomic status was used. Scores of 25-30 were considered a high social status, 20-<25 were regarded as middle social status, 15 to <20 indicated low social status while very low social status was defined at scores <15

Table 2: Univariate analyses for factors associated with post-discharge mortality in 104 severely malnourished children discharged with a follow-up plan

	Censored during or at the end of follow-up (n=97), n (%)	Died during follow-up (n=7), n (%)	HR (95%CI) for post-discharge mortality	P-value*
Time (months)			NA	0.86
12 m	68 (93.2)	5 (6.8)		
12-24 m	25 (92.6)	2 (7.4)		
24 m	4 (100)	0 (0)		
Sex				0.82
Male	46 (93.9)	3 (6.1)	0.84 (0.20-3.58)	
Female	51 (92.7)	4 (7.3)	Reference	
Residence				0.13
Rural	55 (90.2)	6 (9.8)	4.23 (0.53-33.88)	
Urban	42 (97.7)	1 (2.3)	Reference	
Socioeconomic score			NA	0.24
Low social standard	38 (88.4)	5 (11.6)		
Middle social standard	57 (96.6)	2 (3.4)		
High social standard	2 (100)	0 (0)		
Other's education				0.02
Literate	16 (80.0)	4 (20.0)	5.60 (1.63-23.06)	
Uneducated	81 (96.4)	3 (3.6)	Reference	
WZ				0.61
-3SD	80 (82.5)	5 (71.4)	0.56 (0.12-2.67)	
Not < -3SD	17 (17.5)	2 (28.6)	Reference	
IZ				0.78
-3SD	89 (91.8)	6 (85.7)	0.57 (0.08-4.22)	
Not < -3SD	8 (8.2)	1 (14.3)	Reference	
Edema				0.01
Edematous Malnutrition	35 (36.1)	6 (85.7)	9.22 (1.15-73.81)	
Non-edematous Malnutrition	62 (63.9)	1 (14.3)	Reference	
Comorbidity/complication admission				0.59
Complicated	86 (88.7)	6 (85.7)	0.98 (0.82-1.17)	
No complications	11(11.3)	1 (14.3)	Reference	

*The crosstabs command of SPSS with Fisher Exact test was used.

Table 3: Cox regression for factors associated with post-discharge mortality in severely malnourished children admitted to Minia University Maternity and Children Hospital, January to December 2018

	Cases/Total (n)	Crude model ^a		Multivariable model ^b	
		HR (95%CI)	P-value	HR (95%CI)	P-value
Mother's education					
Educated	3/84	Reference	0.01	Reference	0.01
Illiterate	4/20	7.16 (1.60-32.13)		7.10 (1.58-31.93)	
Edema					
Non-edematous malnutrition	1/63	Reference	0.07	Reference	0.07
Edematous malnutrition	6/41	7.04 (0.85-58.50)		6.96 (0.84-57.85)	

^a The crude model included one variable at a time.

^b The multivariable model included the two variables simultaneously.

Figures

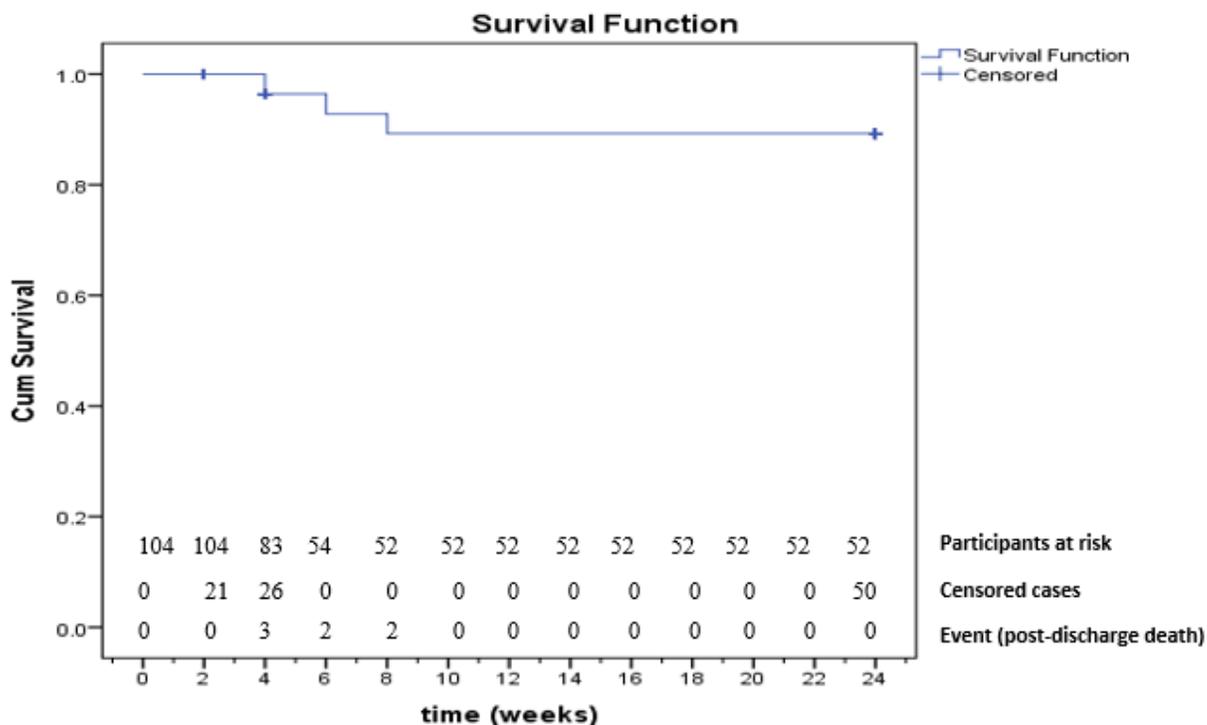


Figure 1

Kaplan Meier survival curve for children discharged and followed up for six months. The blue line represents the cumulative survival function across the follow-up time and the cross signs represent when data were censored and numbers for at risk, censored and events are given in the lower part of the figure.

Supplementary Files

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