Original Article

Efficacy of Ampicillin and Gentamycin Combination Therapy in Children Having Severe Acute Malnutrition Presenting with Acute Diarrhea at Civil Hospital Hyderabad

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ABSTRACT

Objective: To assess the Efficacy of Ampicillin and Gentamycin combination therapy in children having severe acute malnutrition presenting with Acute Diarrhea at Civil Hospital Hyderabad

Study Design: Descriptive / case series study

Place and Duration of Study: This study was conducted at the Paediatric Department, Liaquat University of Medical and Health Sciences Hospital Hyderabad from 1st July 2017 to 31st December 2017.

Materials and Methods: This study was done by Non-probability, consecutive sampling technique in 145 children with the diagnosis of severe under nutrition presenting with acute diarrhea. History and physical examination was carried out. Patients were treated as per the standard guidelines by the WHO and Ampicillin+Gentamycin were given. Weight and height was plotted on the standard growth charts and centiles for age and gender for screening of malnutrition.

Results: The average age of the patients was 14.81±7.67 months. Out of 145 under nourished children 85(58.62%) showed satisfactory outcome at the end of 48 hours of therapy

Conclusion: In conclusion, treatment with intravenous ampicillin and gentamycin showed improvement in only 58.6% children at the end of 48 hours of therapy. Further large scale studies are needed to review the response of these antibiotics in children having Severe Acute Malnutrition with acute diarrhea, hence to review for any possible change in the current protocol.

Key Words: Severe Acute Malnutrition, Children, Antibiotics, Response

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INTRODUCTION

Malnutrition causes about 8 million deaths in under five years old children worldwide.[1] It causes almost half of all childhood deaths in developing countries.[2] Severe acute malnutrition (SAM) is diagnosed if weight-for-height Z-score (WHZ) is <–3 standard deviation in children. SAM is the worst form of malnutrition and it affects 19 million children all over the world.[3]

As compared to other developing countries, Pakistan has the highest prevalence of child malnutrition.[4]

Infectious Diarrhea is responsible for second leading cause of death among less than 5 years old children worldwide (about 1,400 children die every day). It causes more death in children comparing to AIDS, malaria, and measles.[5] The prevalence of diarrhea in Pakistan is 23.8% and its prevalence is more in children under 24 months.[6] In 2016 the prevalence of diarrhea was 12% in children under age 5 years.[7]

World Health Organization (WHO) recommend parenteral Ampicillin and gentamicin as a first line antibiotic therapy for children having complicated severe acute malnutrition including diarrhea.[8] This has led to improvement in mortality rates as shown in studies from different parts of the world. There is 50% decrease in mortality after the implementation of WHO antibiotic protocol for complicated SAM. [9] In some international studies, mortality rates of 4.63% have been observed in malnourished patients treated with recommended oral rehydration formulas and antibiotic regimen recommended by the WHO.[10,11]

Current studies (low quality evidence) suggest increasing antimicrobial resistance to first line antibiotics (Ampicillin and Gentamycin) but evidence for the efficacy of alternative first-line antibiotics are lacking.[12] Because of bacterial resistance to the currently recommended first-line antibiotics effective

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alternatives should be sought. In a study from Uganda only 30% blood cultures were sensitive to ampicillin and Gentamycin. Resistance is a problem in all geographical areas, but there is a lack of recent high quality studies.[13]

In developing countries infectious diarrhea is very common in children having malnutrition and infection related deaths are also very common.[14] Therefore, the management of infection should be more aggressive in these children. Malnourished children with diarrhea are a special subgroup in which administration of antibiotics gains importance due to the immune-compromised state of the child.[15,16]

The aim of this study is to determine the outcome (response) of the children having severe acute malnutrition presenting with acute diarrhea and treated with first line antibiotics (Ampicillin and Gentamycin). This study will help us to develop better protocols to treat these children as there is no local data evidence, and thus lead to improvement in morbidity and mortality. This study itself is a new study in determining the outcome of severely under nourished children who present with acute diarrhea and treated with first line antibiotics as there are no previous studies available.

MATERIALS AND METHODS

This Descriptive Case Series study was done by Non-probability, consecutive sampling technique at Department of Paediatrics Liaquat University of Medical and Health Sciences Hospital Hyderabad in 145 children with the diagnosis of severe acute malnutrition presenting with acute diarrhea from 1st July 2017 to 31st December 2017 (total 6 months' duration). Sample size was calculated by taking proportion of efficacy 60%, confidence level 95%, and margin of error 8%.

Patients of either gender, age 6 months to 59 months who were admitted with the diagnosis of severe acute malnutrition presenting with acute diarrhea as defined in the operational definition were included in the study. Children having the history of chronic diarrhea or other co-morbid conditions or known congenital malformation or any child with severe under nutrition presenting with shock and dysentery were excluded from the study.

Written informed consent to participate in the study was taken from the parents/ guardian of the patient. History and physical examination was carried out. Patients were treated as per the standard guidelines by the WHO and antibiotics (as recommended by the guidelines) were given, that is IV ampicillin 50 mg/kg IV every 6 h and gentamicin 7.5 mg/kg IV once daily. Children having treatment failure, were changed to second-line agents like ceftriaxone 75mg/kg/day OD IV or Ciprofloxacin 20mg/kg/day BID IV.

Age, gender, weight, height and duration of diarrhea were noted. Final outcome was noted. Weight and height was plotted on the standard growth charts and centiles for age and gender was noted. Data was collected on a pre-prescribed Proforma and analyzed using Statistical package for social sciences SPSS version 20. Outcome was considered satisfactory if the frequency of stools was < 3 per 24 hours at the end of 48 hours. Frequency and percentage was calculated for nominal data like, gender and outcome. Mean and standard deviation was calculated for age weight, height duration of diarrhea, weight and height centile. Outcome was stratified for age gender and height weight centile and duration of diarrhea groups. Chi^2 was used and p-value of 0.05 or less was taken as significant.

RESULTS

A total of 145 children with the diagnosis of severe under nutrition presenting with acute diarrhea were included in this study. There were 47.69% children between 6 to 12 months of age, 44.14% were 12.1 to 24 months of age and 8.28% were above 24 months of age as shown in figure 1. The average age of the patients was 14.81±7.67 months similarly mean weight, height, duration of diarrhea and height weight centile is also shown in table 1.

Table1 No1: Demographic Distribution of the Patients n=145

Age	Number	Percentage
6-12 months	69	47.59
13-24 months	64	44.14
>24 months	12	8.28
Gender		
Male	82	56.55
Female	63	43.45
Response to Antibiotics		
Satisfactory	85	58.62
Unsatisfactory	60	41.38
Characteristics	**Mean**	**Std. Deviation**
Age (months)	14.81	7.674
Weight (kg)	5.150	1.4747
Height (cm)	66.45	7.816
Duration Diarrhea (days)	3.05	21.11

There were 82(56.55%) male and 63(43.45%) female as shown in figure 2.

Out of 145 under nourished children 85(58.62%) showed satisfactory outcome at the end of 48 hours of therapy as presented in figure 3. Satisfactory outcome was significantly high in 6 to 12 months of age children (p=0.042) as shown in table 2. It was also significantly high in female patients as shown in table 3. Stratification was also done with respect to height weight centile and duration of diarrhea and found satisfactory outcome with -3 centile and 1 to 5 days'

duration of diarrhea as shown in table 4 and 5 respectively.

indicators. Wasting is most prevalent in Sindh (23.3%) and KP-NMD (23.1%), whereas Gilgit Baltistan and Islamabad have the lowest proportion 9.4% and 12.1% respectively. The prevalence of underweight among children under five years of age is 19.2% in Islamabad and 41.3% in Sindh. [9]Malnutrition is aggravated by diarrhea; one of the leading cause of under-five childhood mortality over last two decades. [17] In malnourished children diarrhea is 5-7 times more common as compared to normal children and it is 3 to 4 times more severe in malnourished children as compared to normal children. Diarrhea continues to be a serious problem in our children

Table No.2: Outcome in Severely Undernourished Children Treated with Intravenous Ampicillin And Gentamycin According to Age Groups

Age Groups (Months)	Outcome		Total
	Satisfactory	Unsatisfactory	
6 to 12	44(63.8%)	25(36.2%)	69
12.1 to 24	38(59.4%)	26(40.6%)	64
>24	3(25%)	9(75%)	12

Chi-Square=6.36 p=0.042

Table No.3: Outcome in Severely Undernourished Children Treated with Intravenous Ampicillin And Gentamycin According to Gender

Gender	Outcome		Total
	Satisfactory	Unsatisfactory	
Male	42(51.2%)	40(48.8%)	82
Female	43(68.3%)	20(31.7%)	63

Chi- Square=4.26 p=0.039

Table No.4: Outcome in Severely Undernourished Children Treated with Intravenous Ampicillin And Gentamycin According to Gender

Height Weight Centile	Outcome		Total
	Satisfactory	Unsatisfactory	
-3	42(73.7%)	15(26.3%)	57
-4 to – 5	43(48.9%)	45(51.1%)	88

Chi-Square=8.78 p=0.003

Table No5: Out Come in Severely Under-nourished Children Treated with Intravenous Ampicillin and Gentamycin According to Duration of Diarrhea

Duration of diarrhea	Outcome		Total
	Satisfactory	Unsatisfactory	
1 to 5 days	85(68%)	40(32%)	125
>5 days	0(0%)	20(100%)	20

Chi- Square=32.86 p=0.0005

DISCUSSION

According to 2018 Pakistan National Nutrition Survey (NNS 2018), 40.2% children under five years of age are stunted while 17.7% are wasted and 28.9% are underweight. Boys are more affected than girls by all forms of malnutrition. Children living in rural areas suffer more from under nutrition than children living in urban areas. Since 1997, the prevalence of wasting among young children is increasing, it was 8.6% in 1997, 15.1% in 2011 and it increased to 17.7% in 2018 (highest rate in Pakistan history). Acute malnutrition remains a nutrition emergency despite the improvement in socioeconomic and is fatal when superimposed upon malnuttrition. [18]

Increasing antibiotic resistance is an issue of international concern. [19] In a study from Bangladesh, only 6 (1.4%) children blood culture isolate was resistant to ampicillin and gentamicin. On the other hand, 3 (0.7%) children blood culture isolates were resistant to ceftriaxone, and 1 (0.2%) was resistant to ciprofloxacin.[20] High rates of non-susceptibility have been documented in several epidemiological studies in children with SAM. [21]

Our Pediatric department has functional nutritional stabilization center for last 10 years and we are dealing with lot of children with Severe Acute Malnutrition having acute diarrhea. Number of Children with acute diarrhea is increasing so no response with first line antibiotics (Ampicillin and Gentamycin) is prolonging the hospital stay of these children and increasing the burden of inpatient children. WHO recommendations regarding the first line antibiotics in complicated SAM should be reviewed to prevent the delay in response in these children.

In our study a total of 145 children with the diagnosis of severe under nutrition presenting with acute diarrhea were included. Gender based provision of medical care is an issue in various developing countries, emphasizing the provision of equal medical care and facilities to boys and girls. [16] Various studies show that South Asian countries has the gender discrimination in health, education nutrition and immunization.[22,23] According to World Bank survey in 2005, there were less health care facilities to girls as compared to boys.[24] In our study we found that there were 56.55% male and 43.45% female showing less number of malnourished female patients as compared to males. This is also supported by the literature which showed food decimation among males and females.[25] An Indian study did not show any gender difference regarding food.[26] The gender of the child was a statistically significant predictor of childhood diarrhea, with boys more likely to be affected by diarrheal disease than girls. This was also supported by various other international studies. [27,28]

In our study the outcome was labeled satisfactory if the frequency of stools was <3 per 24 hours at the end of 48 hours. We found that out of 145 under nourished children 58.62% showed satisfactory outcome at the end of 48 hours of therapy. This satisfactory outcome was significantly high in children between 6 to 12

months of age. Our results are supported by few other studies showing 67% antimicrobial sensitivities of blood culture to the first line combination of ampicillin and gentamicin. [29] While another study showed that 73% organisms were sensitive to gentamicin. [30] Another observational study in Niger done in 311 children aged 6–59 months with complicated SAM. Most isolated Enterobacteriaceae causing diarrhea were resistant to amoxicillin and co-trimoxazole but susceptible to ceftazidime/ceftriaxone, gentamicin and quinolones.[31]

CONCLUSION

In conclusion, treatment with intravenous ampicillin and gentamycin showed improvement in only 58.6% children at the end of 48 hours of therapy. Further large scale studies are needed to review the response of these antibiotics in children having Severe Acute Malany possible change in the current treatment national protocol in SAM children with diarrhea.

Author's Contribution:

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