Determining predictors for severe acute malnutrition: Causal analysis within a SQUEAC assessment in Chad

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The SQUEAC team looking for neighbourhood controls

IRC, Chad

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The authors – especially Casie Tesfai, who conducted the training and supported the fieldwork – would like to acknowledge the contribution of the IRC in Chad, notably Alain Toe, Franck Mpoyi Ntalaja and Dr Ido Charles Gnenassi who were integral members of the SQUEAC assessment team in Mongo District. The IRC team also wishes to thank the support of the MoH in Mongo District, Guerra Region, Chad.

Following the onset of drought in Mongo District, Guerra Region of Chad, in April 2012 the International Rescue Committee (IRC) began supporting the Ministry of Health (MOH) in delivering a community-based management of acute malnutrition programme (CMAM) for the treatment of severe acute malnutrition (SAM). The interventions include an outpatient therapeutic programme (OTP), a stabilisation centre (SC), and a community-based screening and referral programme that employs 200 community health workers to undertake community-based identification and referral of SAM cases.

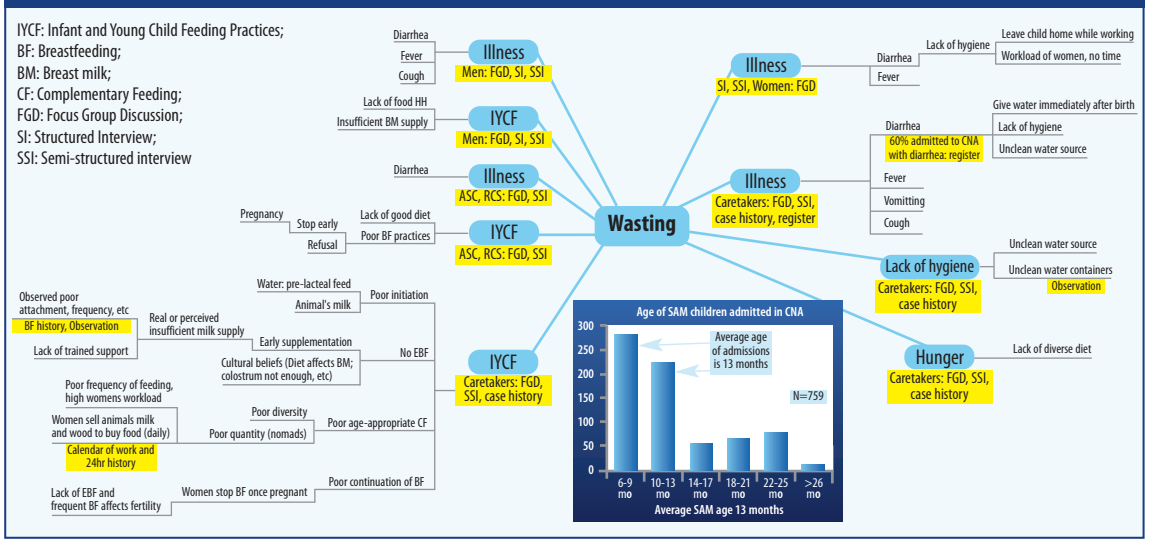
In order to better understand the coverage of the nutrition programme and the factors associated with SAM, in October 2012 the IRC pilot tested the semi-quantitative evaluation of access and coverage (SQUEAC) coverage assessment method together with a causal analysis (i.e. a matched case-control study) of risk factors for SAM in the Mongo District of Chad. This approach to causal analysis within a SQUEAC coverage assessment was piloted by UNICEF Sudan in 2012 and has been documented in *Field Exchange*[1]. The objective of the causal analysis was to identify locally important risk factors for SAM for which focused programming might act to reduce the incidence and prevalence of SAM. Current approaches to causal analysis often include qualitative approaches and a problem-tree analysis. In this article, we discuss the practical application of a more quantitative case-control approach in a rural setting and some of the methodological issues that may require further consideration.

Case–control studies: an old method applied to malnutrition

Case-control studies are commonly used in field epidemiology and seek to compare prior exposures among persons with a condition of interest (cases) and similar persons without the condition of interest (controls). One evaluates whether the ratio of the number with prior exposure (e.g. tampon usage) to the number without prior exposure differs between cases with the condition of interest (e.g. toxic-shock syndrome) and controls without the condition of interest[2]. Case-control studies are *retrospective* studies in the sense that the study starts with disease status and then investigates previous exposures. The strength and the statistical significance of the relationship between the condition of interest and a possible risk factor are described using the odds ratio and the probability (*p-value*) of observing the collected data under the *null hypothesis* of no association. Case-control studies have advantages over other study designs. They are quick and inexpensive. They are ideal for rare conditions (such as SAM) because they start by finding persons who already have that condition rather than hoping that they will turn up in sufficient numbers in a very large sample. Also, several potential risk factors can be assessed simultaneously. Weaknesses of the approach include the difficulty in finding controls that are similar enough to the cases (which can introduce a selection bias) and the need to ask persons to recall prior exposures (which can introduce error and recall bias).

[1] Nyawo M, Myatt M. Causal analysis and the SQUEAC toolbox. Field Exchange 2012;42:37-8.

Figure 1: Mind-map for local hypothesized causes of SAM in Mongo District



Methods

Following the method piloted by UNICEF Sudan, a matched case-control study was conducted alongside the case-finding and data collection done for a SQUEAC stage III coverage assessment. To define the list of potential risk factors, a participatory process was undertaken with programme staff and carers from the CMAM programme. Over a week, a mind-map of potential risk factors was made based on insights gained from analysis of routine programme data and qualitative data from focus groups and key informant interviews with programme staff and carers of SAM cases. The qualitative and quantitative findings were discussed and triangulated to produce a map of potential risk factors and their impact on SAM (see Figure 1). A structured questionnaire was constructed using standardized indicators and question sets from UNICEF and FANTA guidelines[3] that reflected the potential risk factors from the map. The questionnaire was translated into French and back translated to ensure accuracy.

Controls were matched to cases on age (i.e. within ± three months) and neighbourhood, which were considered to be potential confounders. Cases were matched to controls in order to control for confounding and because a smaller sample size is usually needed than when using an unmatched design. A sample size of 40 SAM cases with two matched controls for each case (i.e. 80 controls) was used. Box 1 contains details of the sample size calculations needed for this type of study.

Cases were defined as a child 6 to 59 months of age with MUAC < 115 mm and/or bilateral pitting oedema who was either not enrolled in the CMAM programme or had been enrolled in the CMAM programme for less than three weeks and had lived in the same village for at least two months. Controls were defined as a child of a similar age (i.e. within ± three months) to the case and who had lived in the same neighbourhood of the same village as the case for (at least) the previous two months with a MUAC ≥ 125 mm without bilateral pitting oedema and was not enrolled in the programme.

The sampling of the cases and controls was nested within the SQUEAC stage III coverage assessment. Villages were selected using the centric systematic area sampling (CSAS, quadrat) method. A community case-finding strategy was used in each village to find all current or recovering SAM cases. Once a case was found and his or her carer interviewed, two to three controls meeting the matching criteria were selected and their carers interviewed. Operationally, this meant that one team performed case-finding and interviewed the carers of cases while another team performed control-finding and interviewed the cares of controls.

The data collection team included four IRC health and nutrition staff as supervisors and twelve local staff who spoke French, Arabic and local languages. The questionnaire was kept in French and translated orally into local languages or Arabic as needed, with a common understanding of the expression of terms. The IRC Nutrition Technical Advisor led a three-day training course that focused on interviewing, MUAC measurement and approaches to finding cases and controls. Of the twenty local staff who participated in the training, twelve were selected. The teams field-tested and then modified the questionnaire. During the data collection period, the teams reviewed issues that arose in the field in the evenings. The IRC epidemiologist and Mark

Taking a case history of a SAM child in the OTP to identify possible risk factors for SAM

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Box 1: Sample size calculation

The simplest approach to calculating the sample size required for a case-control study is to use the standard formula for detecting a difference in two proportions:

Sample size in the case group; Mean proportion exposed in cases and controls; Desired power; Significance

$$n = \frac{r+1}{r} \times \frac{(\bar{p})(1-\bar{p})(Z_{\beta}+Z_{\alpha/2})^2}{(p_1-p_2)^2}$$

Ratio of controls to cases; Proportion of cases exposed; Proportion of controls exposed

Common values for power and significance are:

Power	Value
80%	0.84
90%	1.28
95%	1.64
99%	2.33

Significance	Value
20%	1.28
10%	1.64
5%	1.96
1%	2.58

If we want a study with 90% power and 5% significance (these are reasonable values) we have:

$$n = \frac{r+1}{r} \times \frac{(\bar{p})(1-\bar{p}) \times 10.5}{(p_1-p_2)^2}$$

SAM is a rare condition (e.g. only 1% of children may have SAM at the time of a study). This means that it will be much easier to find controls than to find cases. In the sample size calculation presented here, we will assume that we will sample two more controls for each case.

If cases are very rare then we might use more than two cases per control.

We need to decide the size of effect that we want to be able to detect. We do this by specifying an odds ratio. For example, an effect size (odds ratio) of 2.0 is used to detect effects where exposure at least doubles the odds of being a case. In the example sample size calculation presented here we will assume that we want to be able to detect an effect size (odds ratio) of 4.0 or greater.

The table below shows the relation between effect size (odds ratio) and common-sense descriptions of the strength of effect:

Odds ratio		Strength of effect
< 0.1 †	> 10	Very strong
0.10 → 0.33	3.0 → 10	Strong
0.33 → 0.67	1.5 → 3.0	Moderate
0.67 → 0.83	1.2 → 1.5	Weak
0.83 → 1.00	1.0 → 1.2	Very weak / none

† Odds ratios < 1 indicate a protective effect:

Specifying an effect size of 4.0 means that we are interested in detecting strong effects. This strength of effect is useful for identifying targets for intervention. This is because if exposure is common and the effect size (odds ratio) is large then an intervention against the exposure will have a large effect against the disease of interest.

We need to make an informed guess about the proportion that are exposed to the risk factor in the control group. We might be able to inform our guess using data from SMART, MICS, or DHS surveys. If we were interested in diarrhoea in the previous two weeks as a risk factor for SAM we might look at the period prevalence of diarrhoea in non-SAM and non-GAM children in data from a SMART survey. In this example, we made an informed guess that 20% of controls will have had diarrhoea in the previous two weeks. This is p_2 in the sample size formula. We can use the informed guess about the proportion that are exposed to the risk factor in the control group (p_2 = 20%) and the size of effect (odds ratio) that we want to be able to detect to calculate the proportion that will be exposed to the risk factor in the case group (p_1) assuming an odds ratio (OR) of 4.0:

$$P\ exposed\ in\ case\ group = \frac{OR \times P\ exposed\ in\ control\ group}{P\ exposed\ in\ control\ group \times (OR-1)+1} = \frac{4\ (0.2)}{(0.2)(4-1)+1} = \frac{0.8}{1.6} = 0.5$$

and then calculate the mean exposure proportion:

$$mean\ proportion\ exposed = \frac{P\ exposed\ in\ case\ group + P\ exposed\ in\ control\ group}{2} = \frac{(0.5+0.2)}{2} = 0.35$$

We can now calculate the required number of cases:

$$n = \frac{3}{2} \times \frac{(0.35)(1-0.35) \times 10.5}{(0.5-0.2)^2} = 40$$

The number of controls needed is :

$$n_{controls} = 2 \times 40 = 80$$

This sample size (i.e. 40 cases and 80 controls) was used in the causal analysis study reported here.

[2] Shands KN, Schmid GP, Dan BB, Blum D, Guidotti RJ, Hargrett NT et al. Toxic-shock syndrome in menstruating women: association with tampon use and Staphylococcus aureus and clinical features in 52 cases. N Engl J Med. 1980;18;303(25): 1436-42.

[3] USAID, AED, FANTA2, UC Davis, IFPRI, UNICEF and WHO. Indicators for Assessing Infant and Young Child Feeding Practices: Part 2 Measurement. 2010. The exception was the question regarding the introduction of fluids.

Myatt (Brixton Health) provided remote technical support on study design, data-entry, and data-analysis throughout the fieldwork.

Data-entry and data-analysis

Data entry was done on-site by the IRC Nutrition Technical Advisor using Microsoft Excel. Analysis was conducted using STATA 12.0. Conditional logistic regression with backwards elimination of non-significant variables was used. This procedure is appropriate for analysing multivariate data from matched case-control studies. It should be noted that this analysis may also be conducted using free or open-source software (e.g. EpiInfo, R) as was done by the UNICEF team in Sudan[1]. Analysis using STATA was carried out remotely but very soon after data collection.

Findings

The following potential risk factors for SAM were identified and investigated:

- Diarrhoea episode in the previous two weeks (3 or more times per day)
- Fever episode in the previous two weeks
- Pneumonia episode in the previous two weeks (cough and fast breathing)
- Poor treatment seeking behaviour for ill child
- Late initiation of breastfeeding
- Giving food or liquids in the first six months
- Early weaning due to pregnancy
- Household dietary diversity score < 4[4]
- Household Hunger Score ≥ 2 (moderate/severe)[5]
- Unprotected water source

Data collection resulted in a larger sample than anticipated. A total of 62 cases and 157 controls were enrolled. There was an average of about 2.5 controls per case. This resulted in improved power compared to the planned sample size. One case and three controls were excluded because the "case" did not meet the study case-definition.

The age profile of cases (controls) comprised 74.2% (54.8%) aged 6-11m, 22.6% (41.4%) aged 12-23m and 3.2% (3.8%) aged 24-59m. Cases appear to be younger; these age breakdowns are broadly consistent with OTP data on SAM cases. Females comprised a greater proportion of cases (61.3%) compared to controls (45.2%).

Age breakdowns are broadly consistent with OTP data on SAM cases (very few >26 months).Data-analysis revealed two significant associations between fever in the previous two weeks (OR = 7.55, 95% CI = 2.64; 21.62, p = 0.000) and diarrhoea in the previous two weeks (OR = 10.72, 95% CI = 4.27; 26.88, p = 0.000) and being a SAM case.

The infant and young child feeding (IYCF) risk factor 'Giving food or liquids in the first six months' proved problematic as the practice of giving water to neonates before commencing breastfeeding was universal in the study sample. This meant that exposure was identical in cases and controls. Children younger than six months were not included so that it was not possible to employ 24 hour recall.

Discussion

Diarrhoea and fever in the previous two weeks were found to be strongly associated with SAM using a matched case-control study. Integrating this approach within the SQUEAC coverage assessment was shown to be feasible. Planning, training, data collection and data entry for both components (i.e. the SQUEAC stage III survey and the case-control study) occurred simultaneously.

The association between diarrhoea and SAM and between fever and SAM represent multiple causes that contribute, with other factors, to the development of acute malnutrition. Episodes of diarrhoea and fever are consistent with the recorded burden of illness among OTP admissions. Examination of CMAM admissions data, for example, revealed that about 60% of SAM admissions since August 2012 were admitted with diarrhoea.

The study provided evidence that could be translated into action. Recommendations relating to the prevention of diarrhoeal disease and malaria arising from this study include the community-targeted promotion of hygiene, hand-washing, use of ORS, construction and use of protected water sources, the promotion of breastfeeding, and a barriers analysis for breastfeeding (as breastfeeding is likely to be protective for diarrhoea and other infections), the regular use of insecticide treated bed-nets for children under five years of age, and appropriate and early treatment seeking for fever and diarrhoea.

The ability of the matched case-control approach to detect differences based on potential risk factors that do not vary at the community or neighbourhood level (e.g. use of an unprotected water source or a culturally-determined factor affecting IYCF) needs to be considered. Such community and neighbourhood level risk factors will not vary between SAM cases and their neighbourhood controls. Both cases and controls will (e.g.) be exposed to the same unprotected water source. These risk factors will be hidden by the neighbourhood matching process. This prevents any meaningful analysis of these risk factors. During the harvest season where food is more plentiful, dietary diversity and hunger scores may also be similar across households and act as community and neighbourhood level risk factors. An unmatched case-control design may therefore be more appropriate.

As a result of the difficult in identifying and recalling the timing of the disease episode and the onset of malnutrition, the case-control study may only show association and not cause. It is not known (e.g.) whether the case had diarrhoea prior to the onset of SAM or whether SAM came first. Importantly, given the fact that malnutrition increases susceptibility to infection and infection may underlie malnutrition, both episodes may be occurring concurrently and simultaneously[6]. More informative accounts of potential risk factors may be obtained using longer case histories with caregivers in order to determine the sequence of malnutrition and infection. This approach may introduce error or a recall bias. Causal pathways may differ between hunger and harvest seasons. Caution should, therefore, be exercised when generalising results across time. In addition, special attention to cultural practices and the local interpretation of the questions on breastfeeding is important. Importantly, asking IYCF questions for children older than five months inherently requires a recall period of six months or longer and therefore introduces a recall bias.

In summary, the matched case-control study provides a feasible and potentially useful addition to a SQUEAC coverage assessment. While designing effective interventions in nutrition practice is difficult, the identification of risk factors emphasised preventable causes of malnutrition that deserved a specific focus in this programme. The formulation of strong programme responses to investigate and address diarrhoea and fever in the community in an effective way is ongoing.

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Active and adaptive case finding: The SQUEAC team looking for SAM cases in a pastoralist hamlet

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[4] Swindale A, Bilinsky P. Household Dietary Diversity Score (HDDS) for Measurement of Household Food Access: Indicator Guide: version 2. Washington, DC: Food and Nutrition Technical Assistance Project, Academy for Educational Development, 2006.

[5] Deitchler M, Ballard T, Swindale A, Coates J. Introducing a Simple Measure of Household Hunger for Cross-Cultural Use. Washington, DC: Food and Nutrition Technical Assistance II Project, AED, 2011.

[6] Katona P, Katona-Apte J, The interaction between nutrition and infection, Clin Infect Dis. 2008;46(10):1582-8.