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Assessment of the Association Between Fever, Diarrhea, and Cough of Children Under-five in Ethiopia Using Log-linear Model

Etyopya'da Beş Yaş Altındaki Çocuklarda Ateşi Diyare ve Öksürük Arasındaki İlişkinin Log Lineer Model Kullanılarak Değerlendirilmesi

Lijalem Melie TESFAW[a]

[a]Department of Statistics, Bahir Dar University College of Science, Bahir Dar, ETHIOPIA

ABSTRACT Objective: The burden of fever, diarrhea and cough are the three-common leading factors on childhood health. However, it is notable that despite serious symptoms of those children, there remains lack of studies on their association. Therefore, this study is aimed to assess the association between fever, diarrhea, and cough of children under-five in Ethiopia. **Material and Methods:** The data were obtained from 2016 Ethiopian Health Survey (EDHS) data of children under-five. To assess the association between diarrhea, cough and fever, the log-linear model for the three-way table was used. **Results:** A total of 9636 children under-five were considered in the study. About 25.79% of the total children under the study were diagnosed with symptoms of diarrhea, fever or cough. The fitted log-linear model shows that fever was associated with both cough and diarrhea (p-value<0.05). **Conclusion:** The study concludes that fever is significantly associated with both cough and diarrhea. However, there was a lack of a three-way association between fever, cough, and diarrhea which confirms that these three common under-five childhood symptoms have multidimensional nature. Hence, the author would like to recommend for consideration of these three under-five childhood symptoms simultaneously to estimate the actual burden of a childhood health problem as they are not redundant of each other.

Keywords: Diarrhea; fever; cough; log-linear model

ÖZET Amaç: Ateş, ishal ve öksürük yükü çocuk sağlığını etkileyen üç yaygın ana faktör. Fakat bu çocuklardaki ciddi semptomlara rağmen aralarındaki ilişkiyi araştıran çalışmaların sayısının az oluşu dikkat çekicidir. Bu nedenle bu çalışmada Etyopya'da beş yaşın altındaki çocuklarda ateş, ishal ve öksürük arasındaki ilişkinin araştırılması planlanmıştır. **Gereç ve Yöntemler**: Veriler, beş yaşın altındaki çocukların 2016 Etiyopya Sağlık Araştırması (EDHS) verilerinden elde edildi. Diyare, öksürük ve ateş arasındaki ilişkiyi değerlendirmek için, üç yönlü tablo için log-lineer model kullanıldı. **Bulgular**: Çalışmaya beş yaş altı toplam 9636 çocuk dahil edildi. Çalışma kapsamındaki toplam çocukların yaklaşık% 25.79'u diyare, ateş veya öksürük semptomları ile teşhis edildi. Yerleştirilen log-lineer model, ateşin hem öksürük hem de diyare ile ilişkili olduğunu göstermektedir (p-değeri <0.05). **Sonuç:** Çalışma, ateşin hem öksürük hem de diyare ile önemli ölçüde ilişkili olduğu sonucuna varmıştır. Bununla birlikte, ateş, öksürük ve diyare arasında üç yönlü bir ilişki eksikliği vardı, bu da beş yaş altı çocukluktaki bu üç yaygın semptomun çok boyutlu bir yapıya sahip olduğunu doğruluyor. Bu nedenle yazar, bir çocukluk sağlık sorununun gerçek yükünü birbirlerinden gereksiz olmadıkları için tahmin etmek için bu beş yaş altı üç çocukluk belirtisinin aynı anda değerlendirilmesini tavsiye etmek ister.

Anahtar kelimeler: Diyare; ateş; öksürük; log-lineer model

Child health problem is a world-wide concern that needs to give prioritizing to build a quality human resource of the upcoming generation. Even though advance initiatives by government and different stakeholders have taken and children are surviving than ever before globally, yet there are still problems with child health. It is suggested that 16,000 children under-five die every day. In particular, Sub-Saharan countries share the highest weight.[1]

There are numerous types of diseases that children faced when they come-up to this world and till their immunity getting matured to resist antigens. The burden of childhood diseases is high-ranking especially in

Correspondence: Lijalem Melie TESFAW
Department of Statistics, Bahir Dar University College of Science, P. O. Box 79 Bahir Dar, ETHIOPIA
E-mail: lijalemmelie@gmail.com

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developing countries like Africa. Predominantly, globally, the death of children under-five is because of infectious diseases.[2] Of numerous infectious symptoms, diarrhea, cough, and fever are the prominent causes of death.[3] Diarrheal symptoms mainly caused by sunstroke, results from the loss of fluid and electrolytes in diarrheal stools.[4] Contagious of bloody diarrhea is usually characterized by stomach discomfort, and fever.[5] Cough is a brutal exclusion of air from the lung and mostly it is also defined using as inspiratory effort by a forced expiratory effort against a closed glottis consecutively.[6] Normal body temperature of children can vary depending on their age and the time of the day that ranges between 36.5 and 38 ^{o}C. A temperature higher than this is fever, sign of infection in the body.[4]

Clear geographic prevalence difference of childhood fever, cough and diarrhea has been observed in a study which has an implication that it is relevant to deal for different Sub-Saharan countries differently including Ethiopia as well.[4,7] In this sense it can be understood that the distribution might be different even within different parts of the country.

A Nigerian study on common childhood diseases among Nigerian children reported that there are associations between the lack of water, sanitation, and hygiene facilities with the occurrence of fever, diarrhea, and cough. This indicates that a household with the lack of water, sanitation, and hygiene were more likely to suffer from diarrhea, fever, and cough. Fever was the most frequent infectious symptoms followed by diarrhea, and cough.[7] Larger period of diarrhea, fever and cough were linked with larger decreases in weight for age Z-score (stunting) during the observation period.[2] The older the mother gets, the lesser probability of risk of childhood with cough and diarrhea, and the greater the risk of childhood with fever has but the relationship is not consistent in different studies.[7]

Studies reported that childhood morbidity and mortality because of diarrhea, fever and cough have a similar relationship with common children characteristics.[7] This was the motivation for that this research paper which aimed to assess the association between the three most common childhood health problem symptoms. Besides, there are also studies about the burden of diarrhea, fever, and cough separately on children under-five. However, it is remarkable that despite the serious symptoms of those children, there is a lack of tangible study findings on their association. Therefore, this study aimed to assess the association between cough, diarrhea, and fever of children under-five in Ethiopia.

MATERIAL AND METHODS

In this study a total of 9636 valid under five aged children were considered and analysis was carried out. The data were obtained from the 2016 Ethiopian Demographic and Health Survey (EDHS). It is the fourth in a series of demographic and health surveys conducted in Ethiopia in 2000, 2005, and 2011. The sampling frame used for 2016 EDHS was a population and housing census in Ethiopia in 2007. All women aged 15-49 and men aged 15-59 who are the usual members of the selected households are eligible to be interviewed in the survey. One of the main aims of EDHS is gathering and offering data on child health to different researchers' stakeholders and formulate appropriate interventions to counteract fatalities from childhood illnesses and improve the health of children in the country. The sample is stratified and conducted in two stages. The first one to select the enumeration area and the second one to select the household. Stratified sampling technique with proportional allocation was implemented.[8]

In all selected households an information collected from mothers' interviewees aged 15-49 years. In each interviewee of mothers health status of children were obtained by asking the interviewee "Has your child had cough, fever and/or diarrhea in the last 2 weeks?"[8,9] and coded as 1 for response "Yes" and 0 for response "No" for each of the symptom.

ETHICS APPROVAL AND CONSENT TO PARTICIPATE

The ethical clearance for 2016 EDHS was approved by Ethical Review Board, Ethiopia and all participants who agreed to take part in the survey signed a consent form. Hence, the author asked the permission to use data via online form and the data manager gave permission to use for this study.

LOG-LINEAR MODEL

It is used to describe the association in the cross-classification among a set of response categorical variables. Mathematically, it is the natural logarithm of expected frequency. The simplest log-linear model is a model that contains two categorical variables in a contingency table which is also called log-linear model for the two-way table. Consequently, in this study as we have three categorical variables diarrhea, fever and cough symptoms, log-linear model for three-way table was carried out to explore whether significant association exists among the three symptoms.[10]

As log-linear models are examples of generalized linear models (GLM), it treats the cell counts as independent observations from Poisson distribution with corresponding means equal to the expected cell counts.[10,11] Based on our response categorical variables (diarrhea, fever and cough), we would have $2^3+1=9$ log-linear possible models that can be fitted on their structure of association. These nine possible log-linear models of the three variables is revealed in TABLE 1. In the model all possible interactions among the three variables (diarrhea and fever; cough and diarrhea; fever and cough; diarrhea, cough, and fever) were also taken under consideration. The interaction parameters ($\lambda_{ij}^{DF}, \lambda_{ik}^{DC}, \lambda_{jk}^{FC}$ *and* λ_{iik}^{DFC}) are association terms that reflect departures from independence which indicates that the effect of one variable on the expected cell count varies on the level of the other variable.

TABLE 1: Possible log-linear models of three-way table of diarrhea (D), fever (F) and cough (C).

Model	Expression	Description
$\log(\mu_{ijk})=$	$\lambda+\lambda_i^D+\lambda_j^F+\lambda_k^C$	Mutual independence model (pair of variables are independent, both conditionally and marginally)
	$\lambda+\lambda_i^D+\lambda_j^F+\lambda_k^C+\lambda_{ij}^{DF}$	Cough is partially independent of Diarrhea and fever. This model contains the interaction between Diarrhea and Fever.
	$\lambda+\lambda_i^D+\lambda_j^F+\lambda_k^C+\lambda_{ik}^{DC}$	Fever is partially independent of Diarrhea and Cough. This model contains the interaction between Diarrhea and Cough.
	$\lambda+\lambda_i^D+\lambda_j^F+\lambda_k^C+\lambda_{jk}^{FC}$	Diarrhea is partially independent of Fever and Cough. This model contains the interaction between Fever and Cough.
	$\lambda+\lambda_i^D+\lambda_j^F+\lambda_k^C+\lambda_{ij}^{DF}+\lambda_{ik}^{DC}$	Fever and Cough are conditionally independent of Diarrhea. This model contains the interaction terms between Diarrhea and Fever; Diarrhea and Cough
	$\lambda+\lambda_i^D+\lambda_j^F+\lambda_k^C+\lambda_{ij}^{DF}+\lambda_{jk}^{FC}$	Diarrhea and Cough are conditionally independent of Fever. This model contains the interaction terms between Diarrhea and Fever; Fever and Cough
	$\lambda+\lambda_i^D+\lambda_j^F+\lambda_k^C+\lambda_{ik}^{DC}+\lambda_{jk}^{FC}$	Diarrhea and Fever are conditionally independent of Cough. This model contains the interaction terms between Diarrhea and Cough; Fever and Cough
	$\lambda+\lambda_i^D+\lambda_j^F+\lambda_k^C+\lambda_{ij}^{DF}+\lambda_{ik}^{DC}+\lambda_{jk}^{FC}$	Homogenous associations (every variable interacts with each other, but there is no interaction between all three variables)
	$\lambda+\lambda_i^D+\lambda_j^F+\lambda_k^C+\lambda_{ij}^{DF}+\lambda_{ik}^{DC}+\lambda_{jk}^{FC}+\lambda_{ijk}^{DFC}$	All possible interaction between variables

key: $\log(\mu_{ijk})$=log of expected cell counts; D=Diarrhea; F=Fever; C=Cough; $\lambda_i^D, \lambda_j^F, \lambda_k^C$=the effect of diarrhea, fever and cough respectively. Similar for the interaction term. For instance, λ_i^{DF} represent the interaction effect among diarrhea and fever.

GOODNESS OF FIT TEST

The goodness of fit test or model performance evaluation was carried out and depicted in TABLE 5. An estimate in Table 6 is enlightening only if the model fits well.[10] The goodness of fit statistics assess the gap between the observed and model under proposed distribution. The null hypothesis asserts that the gap is only randomly larger than zero which indicates that a given log-linear model holds. The goodness of fit test is used to detected if the reduced model is a better model compared to the saturated (full) model that can be detect using likelihood ratio statistic (G2) and Chi-square statistic ($\chi 2$).[10,11] The larger G2 or $\chi 2$ values are correspondingly smaller p-values indicates poorer fits and gives more evidence against independence. The deviance statistic for logistic models with categorical explanatory variables can also assess goodness of fit of loglinear models by comparing the cell fitted values to the observed counts.[10]

MULTIPLE CORRESPONDENCE ANALYSIS

In addition to log-linear model, multiple correspondence analysis also used to analyze the pattern of relationships of several categorical variables.[12] Particularly, it is attractive and easy to understand over log-linear model to express associations of categorical variables using graphs. Thus, in this paper the association between cough, fever, and diarrhea was also explored using graphs, see FIGURE 1 in the result section.

Data analysis of this study was carried out using SAS software particularly using procedure PROC GENMOD and PROC CATMON and decisions were made using 0.05 level of significance.

RESULTS

Of a total of 9636 children of under-five years of age, the overall prevalence of fever, cough and diarrhea were 1324 (13.74%), 1555 (16.14%) and 1066 (11.06%) respectively, which are revealed in TABLE 2.

TABLE 2: Overall prevalence of fever, cough, and diarrhea in Ethiopia out of 9636 children under-five.

	Fever	Cough	Diarrhea
Frequency	1324	1555	1066

The result in TABLE 2 presented by considering a child has enabled to the victim only one of the three health problem symptoms. In this sense, the symptoms fever, cough, and diarrhea are mutually exclusive to occur on a child. However, in TABLE 3 and TABLE 4, it is indicated that there are children infected by more than one of the three symptoms simultaneously, and hence caution needs to be taken for the interpretation of a total population. For instance, 560 children have both cough and fever. For the sake of simplicity, we present the information in TABLE 3 as TABLE 4.

TABLE 3: Cross tabulation of diarrhea, fever and cough.

			Fever		
Diarrhea			**No**	**Yes**	**Total**
No	Cough	No	7151	284	7435
		Yes	575	560	1135
Yes	Cough	No	479	167	646
		Yes	107	313	420
Total			8312	1324	9636

TABLE 4 shows the categories of children with their corresponding symptoms along with the frequency computed from TABLE 3. In TABLE 4 the sampled children were categorized into none (a child with none of the three symptoms), diarrhea only, cough only, fever only, diarrhea and cough, diarrhea and fever, cough and fever, and finally a child with diarrhea, cough, and fever. This is useful to determine each child in non-overlapping categories because of children enabled to be affected by more than one symptom simultaneously. The prevalence proportion of children with a cough only, nearly 6% of the total, was the highest compared to other categories of infected children. Whereas, children with cough and fever ranked as the second-highest proportion of prevalence. The prevalence of children with diarrhea and cough, on the other hand, was the lowest (1.11%) compared to other categories of infected children.

Therefore, 25.79% (={4.97+ 5.97+2.95+1.11+1.73+5.81+3.25}%) of children were diagnosed with three symptoms which indicates that 25.79% of children were affected by diarrhea, fever, or cough.

TABLE 4: Non-overlapping categories of children under-five with symptoms diarrhea, fever, and cough in Ethiopia.

Category	Frequency (%)
None	7151 (74.21)
Diarrhea only	479 (4.97)
Cough only	575 (5.97)
Fever only	284 (2.95)
Diarrhea and Cough	107 (1.11)
Diarrhea and Fever	167 (1.73)
Cough and Fever	560 (5.81)
Diarrhea, Cough and Fever	313 (3.25)

Prior to fitting the model and the estimation of the parameters, goodness of fit test needs to be checked. The goodness of fit test of the models of diarrhea, fever and cough using Deviance Pearson chi-square (χ^2) and likelihood ratio (LR) statistics were represented in TABLE 5.

A p-value less than the significant level (0.05) for the fit statistics indicates that there is a stronge evidence against the model. On the other hand, the reverse is true that if the p-value is greater than 0.05, it is a strong evidence that the model fits the data well. The p-values of the goodness of fit statistics of Model 1 to 8 are much less than 0.05 level of significance indicating that the models do not fit the data well, while for Model 9 the p-value is equal to 1.00 which is much greater than 0.05 indicating that Model 9, the saturated model, fits the data well. Hence, the model fitting the data well is identified (i.e saturated model) and the parameters were estimated (TABLE 6).

TABLE 5: Goodness of fits tests for log-linear models of diarrhea (D), fever (f) and cough (c)

						p-value	
Model	**log linear model**	**Deviance**	**LR**	**Chi**	**Df**	**LR**	**Chi**
1	(D,F,C)	138.25	2899.06	5368.23	4	< 0.0001	< 0.0001
2	(DF,C)	123.20	2167.86	2860.07	3	< 0.0001	< 0.0001
3	(D,FC)	88.05	797.57	1046.76	3	< 0.0001	< 0.0001
4	(F,DC)	132.11	2513.16	3220.15	3	< 0.0001	< 0.0001
5	(DF,DC)	98.09	1781.96	2541.61	2	< 0.0001	< 0.0001
6	(DF, FC)	34.69	66.37	84.79	2	< 0.0001	< 0.0001
7	(FC,DC)	62.15	411.67	626.50	2	< 0.0001	< 0.0001
8	(DF, DC,FC)	13.98	39.31	42.13	1	< 0.0001	< 0.0001
9	(DFC)	0.000	0.000	0.000	0	1.000	1.000

key: LR=Likelihood Ratio; chi=χ^2 (Pearson chi-square); Df= degree of freedom; D=Diarrhea; F=fever; C=Cough.

The parameter estimates of the saturated model were revealed in TABLE 6. The null hypothesis of each the interaction term claims that there is no interaction among the two symptoms (categorical variables). Consequently, there is a significant interaction between diarrhea and fever (diarrhea*fever); and fever and cough (fever*cough) because the p-value of the estimated coefficient of interaction term is <0.0001, which is much less than 0.05. This refers that the estimated odds between diarrhea and fever (exp(1.0998)=3.004)); fever and cough (exp(-3.1996)=0.0408)) were significantly differ from 1.0 with p-values < 0.0001 which indicates that there is an association between the two under five childhood symptoms. However, in the last two rows, the saturated log-linear model shows lack of association between diarrhea and cough as the p-value is equal to 0.6562 (greater than 0.05), and there was also lack of three way association between diarrhea, fever and cough (p-value=0.8680>0.05).

TABLE 6: Parameter estimates for the saturated log linear model for diarrhea, fever, and cough.

Parameter	Estimate	Standard error	Chi-Square	p-value
Intercept	6.3544	0.0417	23217.4	< .0001
Diarrhea	-1.6815	0.1053	255.08	< .0001
Fever	-1.0218	0.1154	78.42	< .0001
Cough	2.5206	0.0433	3381.43	< .0001
Diarrhea*Fever	1.0998	0.1267	75.29	< .0001
Fever*Cough	-3.1996	0.0848	1424.67	< .0001
Diarrhea*Cough	-0.0264	0.0594	0.21	0.6562
Diarrhea*Fever*Cough	1.0725	51.36	0.01	0.8680

In addition to the estimated parameter in TABLE 6, the association among the three symptoms can also be presented in the figure, see FIGURE 1. FIGURE 1 shows the multiple correspondence analysis of the three common children under-five health problem symptoms. The figure suggests that there is a visible association between fever and cough as indicated in the second as well as fourth quadrants. Moreover, fever is placed on the boundary line and shows that it is associated with both cough and diarrhea which is also in line with results in TABLE 6 testifying a significant association between diarrhea and fever (p-value<0.05). However, there is no association between cough and diarrhea as it is in the second and fourth quadrants which is consistent with the reports obtained from TABLE 6.

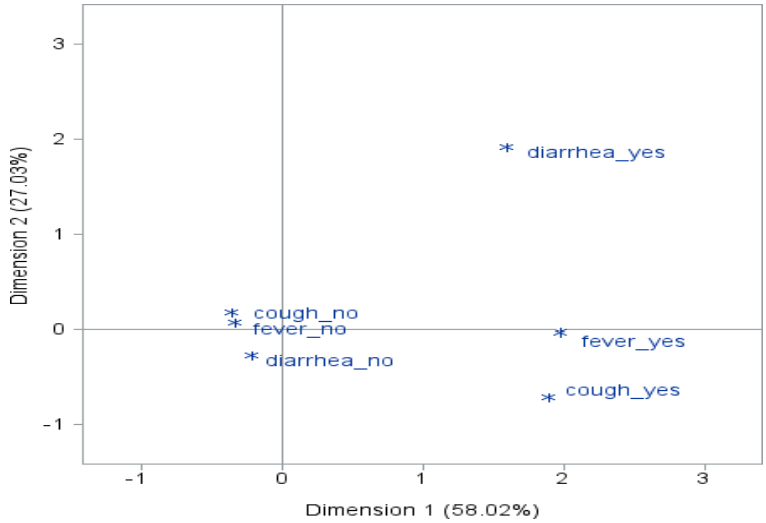

FIGURE 1: Plot of multiple correspondence analysis of fever, diarrhea, and cough of under-five age children in Ethiopia.

DISCUSSION

In this study, the association between diarrhea, fever, and cough symptoms of children under-five was assessed using a log-linear model. In the log-linear model, the association among the three health problem symptoms was represented using the interaction term. Beyond the pairwise association, log-linear model was used to assess the three-way interaction. [10,11] The expected cell counts of diarrhea, fever, and cough were well fitted by the saturated log-linear model (p-value>0.05) as compared to the rest of the unsaturated log-linear model (p-value<0.05).

In this study, the occurrence of children under-five who are vulnerable to cough, diarrhea and fever was high compared to the intentions that the world has committed for the burden of child health problems.[7] The proportion of prevalence of children under-five with cough was in the first highest rank and children under-five with cough and fever were in the second-highest rank. Unlike the findings in the study , fever is the most prevalent of the three symptoms followed by diarrhea and cough, in this study cough is the most frequent followed by diarrhea and fever.[7] In the fitted model as well as from multiple correspondence analysis plots of diarrhea, fever, and cough it was observed that fever significantly associated with cough. These findings of the study are partially consistent with study which states that a cough is associated with fever.[12]

Similarly, it was also indicated that a significant association between fever and diarrhea exists in this study which is in line with studies which testifies the coexistence of the two symptoms.[2,13,14] In a study, it is reported that more days of fever and diarrhea was associated with wasting and underweight.[2] On the other hand, both fever and diarrhea symptoms are important risk factors of anemia.[13] Infectious agents remain the most common causes of acute diarrhea and fever.[14] Moreover, in the study, it was also reported that bloody diarrhea is usually associated with stomach discomfort and fever.[5]

CONCLUSION

The findings of this study conclude that fever is considerably associated with both cough and diarrhea. This does not imply one fever indicator causes the other since cross-sectional data were used for the analysis and other factors were not taken into consideration whereas there is no significant association between cough and diarrhea. Moreover, the study reported that there is no three-way association between diarrhea, fever, and cough. From the lack of three-way interaction, one can conclude that those three commons children under-five symptoms have multidirectional nature. Hence, the stakeholders need to consider the three-childhood symptom parallelly to approximate the definite burden of children health problem as they are not redundant of each other. In the end, the author would like to recommend a possible future study to assess the causal relationship among the three common childhood symptoms using retrospective as well as prospective sampling design.

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Conflict of Interest

No conflicts of interest between the authors and / or family members of the scientific and medical committee members or members of the potential conflicts of interest, counseling, expertise, working conditions, share holding and similar situations in any firm.

Authorship Contributions

This study is entirely author's own work and no other author contribution.

Availability of Data and Material

The datasets for generated analyses during the study is available in Ethiopian Demographic and Health Survey data if unique request sent via their site EDHS 2016.

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