# Association of *Nuzj* (Concoction) appearance with Biochemical Parameters and Personal Characteristics in cases of *Daul-Feel* (Lymphatic Filariasis)

**Anirban Goswami¹\*, Md Ishtiyaque Alam¹, Mahboob-us-Salam², Najmus Sehar²**

¹Regional Research Institute of Unani Medicine, Patna (CCRUM, Ministry of Ayush, India)
²Central Research Institute of Unani Medicine, Lucknow (CCRUM, Ministry of Ayush, India)

**ABSTRACT:**

*Daul-Feel* (Lymphatic Filariasis) is characterised by swelling of the feet and calf in which the affected leg becomes extremely swollen in advanced stage which resembles the leg of an elephant. According to the Unani System of Medicine, this disease cause by the derangement of temperament or humours like, *Bulgham*, *Safra* and *Sauda*. *Nuzj* (concoction) is the process through which the consistency of morbid matter is changed by the administration of *Munzijat* (concoctive) of respective humour or temperament to make it easy to be removed from the body. The aim of this study to find out the significant factors as Biochemical Parameters and Personal Characteristics associated with the *Nuzj* (concoction) appearance in urine. Patients registered at RRIUM, Patna and complaining of the limb swelling with present or post history of limb redness were screened for the clinical evidences of the disease. UNIM-MUNB (*Munzij*) was administered to the patients for 10 to 15 days according to chronicity of disease or till the appearance of *Nuzj* in the urine. GLM model used to determine the association of biochemical parameters and personal characteristics with the *Nuzj* appearance days in urine. This study concluded that *Nuzj* associated with the Age, Sex and Biochemical Parameters in cases of *Daul-Feel* (Lymphatic Filariasis).

**KEY WORDS:** Association, *Daul-Feel* (Lymphatic Filariasis), Generalized Linear Model (GLM), Geometric distribution, *Nuzj* (Concoction).

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**INTRODUCTION:**

Filariasis (*Daul Feel*) is the name given to a collection of tropical disorders caused by thread-like parasitic round worms (nematodes) and their larvae. A mosquito bite transmits the disease from the larvae to people. *Dual Feel* (Lymphatic Filariasis) is also known as elephantiasis. A patient leg looks like a leg of an elephant. The name of the disease is feel-pa[1]. This disease characterized by fever, chills, headache, and skin lesions in the early stages and it can progress to include gross enlargement of limbs. Filariasis is one of the country's top objectives, and researchers from all over the world are working to eradicate the

illness. The World Health Assembly resolved in 1997 to eliminate lymphatic filariasis as a public health problem. The goal of the World Health Organization's (WHO's) 'Global Programme to Eliminate Lymphatic Filariasis (GPELF)' is to eliminate the disease as a public health problem by 2020[2]. India has set its target for national elimination by the year 2015[3].

In Unani system of medicine Lymphatic filariasis is known as *Daul Feel*. *Daul Feel* is defined as a swelling of feet and calf in which the affected leg becomes widely swollen in advanced stage which resembles the leg of an elephant. Therefore, it's known as *Daul Feel*. In addition, this disease is caused by accumulation of *Balgham-e-Ghaleez* in the affected part. This *Balgham-e-Ghaleez* converts into *Sawda* on becoming chronic which is known as *Sauda-e-Balghami*[4]. The skin of the feet and calf is reddish in the acute stage of the disease and eventually becomes black closed to bluish as the disease progresses. According to the Unani System of Medicine, this disease cause by the derangement of temperament like, *Bulgham*, *Safra* and *Sauda*. In modern medicine, Diethylcarbamazine (DEC) is the only drug available for therapeutic control of filariasis[5], but this drug has varying efficacy and serious allergic reactions while Unani medicine is safe and efficacious. Unani physicians have suggested that treatment for Lymphatic Filariasis should be started with the evacuation of Phelegm and black bile (*Balgham* and *Sawda*) from the human body for *musleh* and *tadeel-e-mijaz* (Correction of *mizaj* or temperament). The commonest mode or method of *Istifragh* for the excretion of B*algham* and *Sawda* is *Munzij wa Mus'hil* therapy (Concoctive and Purgative) which is followed by three steps. [6]

1. Use of *Munjizate Balgham* and *Sawda*. (Phlegmatic and Melacholic Concoctives)
2. Use of *Mus'hilat-e -Balgham* and *Sauda*. (Melacholic and Phlegamatic Purgative)
3. *Tabreed-e-Badan* (Refrigeration of body)

These above therapies were given orally once a day on empty stomach in the morning for 10 to 15 days according to chronicity of disease or till the appearance of *Nuzj* (concoction) in the urine. *Nuzj* (concoction) is the process through which the consistency of morbid matter is changed by the administration of *Munzijat* (concoctive) of respective humour or temperament to make it easy to be removed from the body. [7-9] Sometimes the matter is too thick or too thin to be eliminated; therefore, *Munzijat* drugs are used which change the consistency of the humour and make it readily suitable for elimination.

Actually, *Nuzj* is a natural process that occurs in the body and it is the function of innate heat. It happens in the stomach, liver, and organs in response to dietary digestion. This procedure necessitates the optimal innate heat of organs, if any deviation occurs in innate heat of organs due to accumulation of abnormal matter in organs, there is dire need of help of physician to use such drugs which can help in the process of *Nuzj*. As a result, tabiyat (which is a supreme planner of the body to create the healthy environment within the body and prepare to fight against the disease) dominant on matter.[10] and it can be eliminating with the help of expulsive power. [11] As a result, the *Nuzj* process aids in the easy evacuation of causative materials from the body and it plays an important role in the elimination of waste materials that are responsible for disease causation. [12]

*Nuzj* (Concoction) is required in the treatment of all chronic disorders as well as

disorders lasting more than 40 days. As per the method of treatment given in Unani classical books *Nuzj* (Concoction) is a must in chronic ailments, but optional in acute diseases depending on the severity and acuteness of the condition. [13,14] Appearance of the *Nuzj* in urine may be associated with Biochemical Parameters and other Characteristics of the patients. Therefore, our objective of this study to find out the significant factors (as Biochemical Parameters and Personal Characteristics) associated with the *Nuzj* (concoction) appearance in urine using statistical model of lymphatic filariasis patients. Remaining part of this paper has been organized as follows, in section 2, we describe the Material and Methods. Section 3 and Section 4 describe as Statistical Methodology and Statistical Results and Graphical Analysis and Section 5 as discussion. Finally, in section 6 we conclude the article.

### MATERIAL AND METHODS:

This study was conducted by Regional Research Institute of Unani Medicine (RRIUM), Patna (CCRUM, M/O AYUSH, New Delhi) during April 2008 and March 2014. This study protocol was approved by the Institutional Ethical Committee of RRIUM, Patna during 2012-13. Patients of *Daul Feel* (lymphatic filariasis) of either sex aged between 18-65 years having lower lymph oedema and having one or more symptoms such as fever with and without rigour, lymphadadenitis, dermatosclerosis, lymphangitis and headache were selected for the study from OPD, after thorough clinical examination by Unani physician. Patients, who were suffering from other systemic disease, anaemia, malnutrition and pregnant and lactating women were excluded from the study. Patients were registered in this study with consent of patients and duly signature by informed consent form. In this study, patients were administration with UNIM-MUNB (*Munzij*) adult dose (1 packet) boiled in 350 ml of water for 15 minutes added with 20 grams of honey (only in non-diabetic cases). The prepared decoction was given orally once a day on empty stomach for 15 days or till the appearance of *Nuzj*. The patient's characteristics like their age, occupation, dietary habits, duration of the disease, symptoms suggesting disease, frequency duration and bio-pathological parameters were recoded. A total 73 of 79 patients included in this study who have appeared *Nuzj* within 15 days. The description of the significant covariates, factors and their levels with the summarized statistics such as the mean, standard deviation, range and proportion of the levels are provided in Table 1.

### STATISTICAL METHODOLOGY:

We consider how many days taken to appearance of the *Nuzj* in a patient as our response variable, that is, $Y_i = i$, where i denotes appearance of the *Nuzj* at days i. Suppose, $Y_i$ = number of failures needed to get the 1st success or number of events before the 1st occurrence of the event of interest follows the geometric distribution. So, our response variable follows the geometric distribution. So, this study is an attempt to find the significant factors associated with the response variable by using the Generalized Linear Model (GLM) for the geometric distribution.

Suppose, p be the probability of success on each trial, then the probability that $y_i$ failures are needed to get one success is

$$f(y_i, \Theta) = pq^{y_i-1} \qquad (1)$$

where $y_i$ = 1, 2, 3, ... and p + q = 1. The mean and variance of Equation (1) are E(Y) = μ =

$\frac{1}{p}$ and $Var(Y) = \mu(\mu - 1) = \frac{q}{p^2}$. the geometric distribution can be obtained from negative binomial distribution when the number of successes, r = 1[15].

Now, we can express that equation (1) follows exponential family of distribution with natural parameter g(θ)= ln (1 – p) , which yields the link function of the GLM as

$$\gamma(\mu_i) = \ln\left(\frac{\mu_i - 1}{\mu_i}\right), \qquad (2)$$

where, $\mu_i = \frac{1}{1 - e^{\eta_i}}$ , $\eta_i = \mathbf{X}_i'\boldsymbol{\beta}$ , **X** and **β** are vectors of covariates and parameters, respectively. The parameters or regression coefficients **β=** (β1, β2, ..., βk) are unknown parameters that are estimated from a set of data. Then the log link function can also be used to fit the GLM for the geometric distribution [16,17]. So, that the geometric of random variable $Y_i$, log link function can also be used. The log-link function is

$$\mu_i = e^{\mathbf{X}_i'\boldsymbol{\beta}} = e^{\eta_i} \qquad (3)$$

or, $E(Y_i) = e^{\eta_i}$

Similarly, the natural link function is $E(Y_i) = \frac{1}{1 - e^{\eta_i}}$
where, $Y_i$ = i, where i denotes appearance of the *Nuzj* at days i.

In this present study, the results using log-link function and the natural link function from the likelihood function of the geometric distribution are compared. This comparison is told us whether use of log link function should be preferred to the natural link function while fitting the GLM of the geometric distribution. The geometric distribution may be obtained from the negative binomial distribution when the number of success, r = 1, for modelling the response variable of interest in present study, log link function may be used with its corresponding estimates in (6) and deviance. We see log link or natural link function are frequently used for the GLM of negative binomial distribution and it is functioned by in built in function of 'glm' with family: negative. binomial, parameter: theta = 1 and link: "log" or "identity" of R-Programming Language (version 4.1.0). [18-21]

**Table- 1: Summary Statistics of variables in the analysis:**

| Variable | Abbreviation of variable | Mean ± SD / Frequency (%) | Range |
|---|---|---|---|
| *Nuzj* appearance days | *Nuzj* Days | 8.41 ±2.58 | 1-15 |
| Age of the patient (Year) | Age | 38.64 ±14.28 | 12-62 |
| Gender (Male=1, Female=2) | Sex | 1=M=32 (43.84%) 2=F=41(5616%) | |
| Absolute Eosinophil Count | AEC | 433.5±207.49 | 130-950 |
| Globulin | GLO | 2.60±0.65 | 1.4-5.2 |
| Erythrocyte Sedimentation Rate | ESR | 26.66±30.50 | 20-138 |
| Total Protein | TP | 6.60±0.83 | 4.2-10 |
| Monocytes | M | 1.41±0.84 | 0-4 |

**Table-2: Estimates of parameters of GLM of the geometric distribution for *Nuzj* appearance:**

| Model | Covariate | Estimate | Standard Error | t-value | p-value | AIC |
|---|---|---|---|---|---|---|
| GLM (Natural link) | Intercept | 10.37358 | 2.047711 | 5.06594 | <0.001 *** | 380.34 |
| | ESR | -0.02187 | 0.007632 | -2.86523 | 0.006039 ** | |
| | TP | -0.7162 | 0.284865 | -2.51416 | 0.015129 * | |
| | M | 0.748442 | 0.30851 | 2.425987 | 0.018843 * | |
| | Age*Sex-F | 0.032292 | 0.020803 | 1.552299 | 0.126775 | |
| | Age*Sex-M | 0.033459 | 0.018375 | 1.820886 | 0.074493. | |
| | AEC*GLO. | 0.000775 | 0.000451 | 1.716251 | 0.092185. | |
| GLM (Log link) | Intercept | 2.358362 | 0.269666 | 8.745487 | <0.001 *** | 380.31 |
| | ESR | -0.0031 | 0.001067 | -2.90194 | 0.005464 ** | |
| | TP | -0.08943 | 0.039653 | -2.25539 | 0.028429 * | |
| | M | 0.085072 | 0.037827 | 2.249012 | 0.028859 * | |
| | Age*Sex-F | 0.0046 | 0.00258 | 1.783139 | 0.080515. | |
| | Age*Sex-M | 0.004607 | 0.002247 | 2.049936 | 0.045529 * | |
| | AEC*GLO. | 0.000102 | 5.43E-05 | 1.881937 | 0.065557. | |

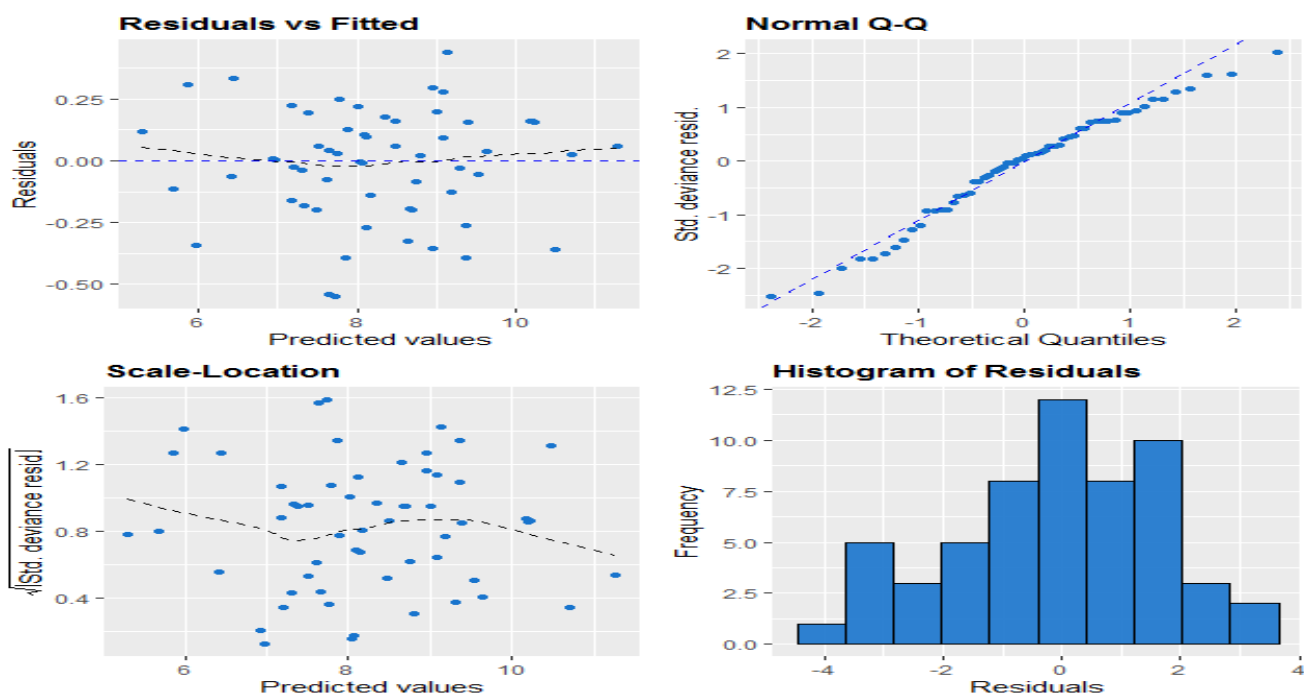Level of Significant define as '***'< 0.001, '**' < 0.01, '*' < 0.05, '.' < 0.1



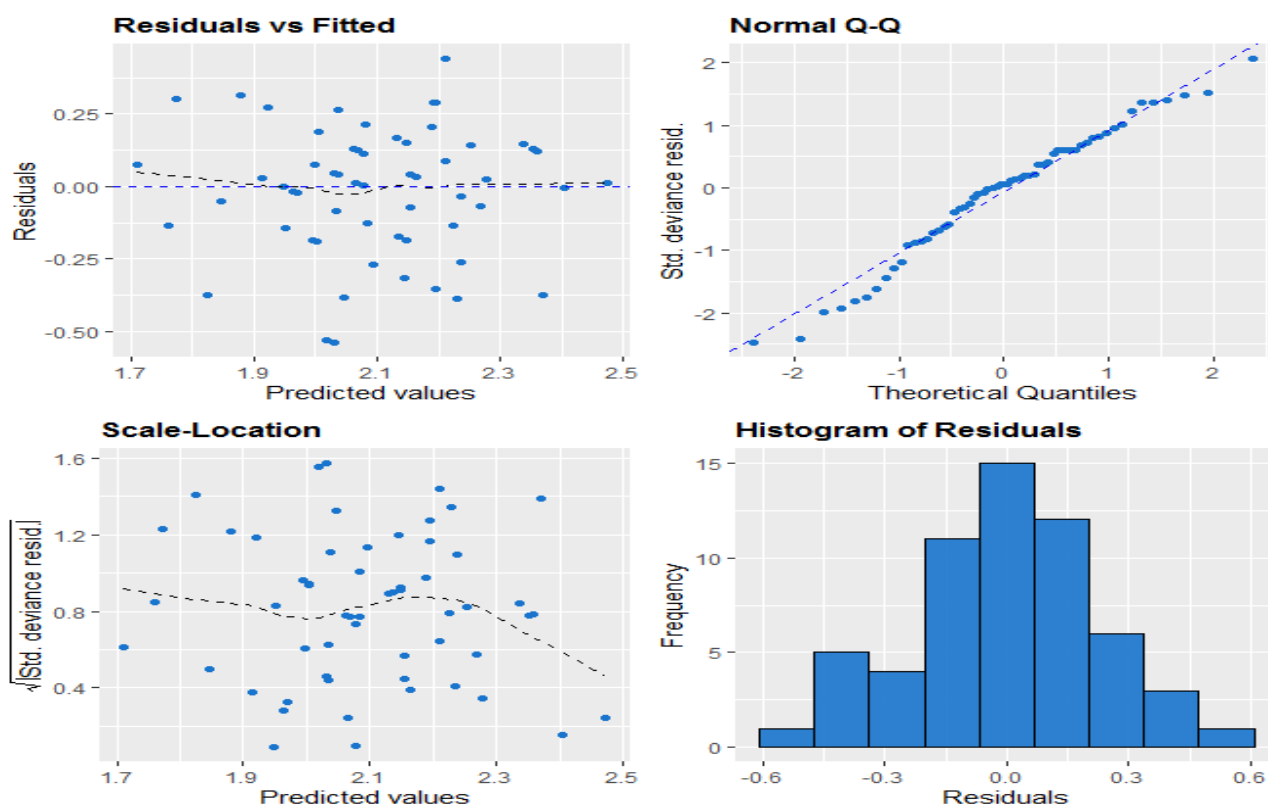**Figure 1:** Model diagnostic plot for the GLM of the geometric distribution with Natural link

**Figure- 2:** Model diagnostic plot for the GLM of the geometric distribution with log link

## RESULTS AND GRAPHICAL ANALYSIS:

In this study, GLM regression modeling techniques have been carried out to study the impact of *Nuzj* appearance day along with the others cofactors of the patients like demography and bio-path characteristics. Firstly, we modelled the response variable *Nuzj* appearance through GLM adopting the geometric distribution with 'natural' and 'log' link. The best models will be finalized based on the smallest AIC. [22] Also, the separate diagnostic plot for these two models are taken into account for model selection. Fig. 1 and 2 represent the residuals vs fitted, Normal Q-Q of residuals, scale-location and histogram of residuals plot of the GLM models respectively.

Both figures displays the straight flat diagram for residual vs fitted, implying that the variance is constant with running means. Normal probability plot for standard residuals shows that the almost in $45^0$ for both of models. From these figures, it can be interpreted that there is no lack of fit or departure from symmetricity.

*Nuzj* appearance days GLM geometric fitted mean ($\hat{\mu}$) model with natural link (from Table 2)

$\hat{\mu}=1/\{1-\exp$ (10.373-0.021 ESR-0.716 TP+0.748 M+0.032 (Age*SexF)+0.033 (Age*SexM)+0.0007 (AEC*GLO)}

and, with natural link as

$\hat{\mu}=\exp$ (2.358--0.0031 ESR--0.089 TP+0.085 M+0.0046 (Age*SexF) + 0.0046 (Age*SexM)+ 0.0001(AEC*GLO)

In Table 2, summarized forms of the obtained GLM geometric fitted models of *Nuzj* appearance are given. Therefore, the

following interpretations are drawn based on the GLM geometric with Natural link.

1) The *Nuzj* is negatively associated with ESR with p-value < 0.01, which indicates that if ESR level in the blood increases *Nuzj* appearance days decreases.

2) The *Nuzj* is negatively associated with TP with p-value < 0.05, which indicates that if TP level increases *Nuzj* appearance days decreases.

3) The *Nuzj* is positively associated with M with p-value < 0.05, which indicates that if M level rises a *Nuzj* appearance days increases.

4) *Nuzj* appearance is positively jointly marginally positively associated with age and male sex with p-value 0.074.

5) *Nuzj* appearance is positively marginally associated with the interaction effect (AEC*GLO) with p-value 0.09, indicating that *Nuzj* appearance increases as (AEC*GLO) also increases. This situation implies that AEC and GLO jointly increases the *Nuzj* appearance.

Similarly, from Table 2 for GLM geometric with log link

1) The *Nuzj* is negatively associated with ESR with p-value < 0.01, which indicates that if ESR level in the blood increases *Nuzj* appearance days decreases.

2) The *Nuzj* is negatively associated with TP with p-value < 0.05, which indicates that if TP level increases *Nuzj* appearance days decreases.

3) The *Nuzj* is positively associated with M with p-value < 0.05, which indicates that if M level rises a *Nuzj* appearance days increases.

4) *Nuzj* appearance is positively jointly positively associated with Age and male sex with p-value <0.05, but marginally significant with female p-value 0.080.

5) *Nuzj* appearance is positively marginally

associated with the interaction effect (AEC*GLO) with p-value 0.06, indicating that *Nuzj* appearance increases as (AEC*GLO) also increases. This situation implies that the AEC and GLO jointly increases the *Nuzj* appearance.

It is also observed that, the both of GLM fitted model has same AIC value 380.34 and 380.31 respectively. But, the GLM for the geometric using log link provides maximum significant variables.

**DISCUSSION:**

In this article, association between *Nuzj* (concoction) appearance in urine with biochemical parameters and personal characteristics of Lymphatic Filariasis patients has been studied. Because, the geometric distribution contributes significantly to express many important facts associated with the 1st occurrence of any event. Also, *Nuzj* appeared in a particular day in urine follows the same distribution. In this study, the GLM for the geometric distribution used to determine the causal parameters for appearing the *Nuzj*. Two different generalized linear models are fitted, one using the natural link function and the other one using the log link function. Also, a comparison of the GLM for the geometric distribution using natural and log link function has been made in this study. The model diagnostic plot (Fig. 1 and 2) showed that the straight flat diagram for residual vs fitted, indicate that the variance is constant with running means. Also, normal probability plot for standard residuals was almost in $45^0$ for both of models. So, we may conclude that there is no lack of fit or departure from symmetricity. It is noted that, the both of GLM fitted model has same AIC value. In GLM geometric distribution with natural link and log link of *Nuzj* appearance is expressed by, ESR, TP, M, Age*Sex-F,

Age*Sex-M, AEC*GLO. Here things to be noted that the natures of marginal effect of Age*Sex-M, AEC*GLO and Age*Sex-F is insignificant and ESR, TP and M are significantly associated with *Nuzj* appearance for natural link model. Similarly, ESR, TP, M and Age*Sex-M are significantly associated, where Age*Sex-F and AEC*GLO are marginally associated *Nuzj* appearance for log link model. From these models it is conclusive that ESR and TP has negative impact, where M, Age and Sex has a positive impact on *Nuzj* appearance.

**CONCLUSION:**

In this study biochemical parameters and personal characteristics such as total protein, monocyte, ESR, age and Male-sex were significantly associated but age and Female-sex was marginally associated with the *Nuzj* appearance in urine (p-value <0.05) whereas AEC and Globulin have found marginally significant (p-value=0.065) result.

**LIMITATION OF STUDY:**

The analysis of this study was done with 79 patients. If the sample size was large, then the more parameters may be significantly associated with *Nuzj* appear.

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