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RESEARCH ARTICLE

Modified Bayesian survival analysis of Diabetes Mellitus in selected hospital facilities in Nasarawa, Nigeria

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Abstract

Diabetes mellitus is a global chronic health problem affecting over 400 million people. The study focused on the commonest type of Diabetes-Type II diabetes. The disease is associated with morbidity and mortality. Bayesian survival model may be utilized to assess the risk factors associated with Diabetes. The study utilized secondary data from 532 diabetic patients from two General Hospital facilities in Nasarawa State, Nigeria. The aim of the paper was to apply a Bayesian survival model on diabetic dataset to assess some risk factors pertaining to the disease. This Bayesian model was modified to Diabetic Additive Models (DAMS) and further extended to the Diabetic Additive Constant Hazard Model (DACHM), the coded version C. DACHM (when all metrical covariates were coded) and Diabetic Additive Accelerated Failure Time Model (DAAFTM). The results show that C.DACHM outperforms the other model with least values of Watanabe Akaike Information Criterion (WAIC), Deviance Information Criterion (DIC), and a large predictive power measured by the Log Pseudo Maximum Likelihood (LPML). The C.DACH model suggests that; good management of type II diabetes patients aged 40 years and above in both hospitals reduced the risk of death. Considerably, low Body Mass Index (BMI) increased the risk of death of patients with the disease. Body Mass Index, BMI greater than 24.9 (overweight) are 5.41E-17 times at risk of death from diabetes than those of normal weight. High Systolic Blood Pressure, SBP, greater than 140 (high) increases the risk of dying from the diseases by 1.51 times than those of normal SBP. High Diastolic Blood Pressure, DBP, greater than or equal to 90 (high) increases the risk of dying from the diseases by 7.81 times than those of normal DBP. Male patients were 1.28 times at risk of death from diabetes than their female patients. Patients of General Hospital Keffi experience are 1.02 times at risk of death than those of the General Hospital Nasarawa. The research recommends patients' drug compliance especially for patients above 40 years, maintenance of a healthy body mass index and maintenance of a healthy blood pressure.

Keywords: Diabetes, Bayesian Survival Model, Proportional Hazard, Accelerated Failure Time Model, Additive Model.

1.0 Introduction

Diabetes Mellitus (DM) or Diabetes is a chronic metabolic disorder characterized by elevated levels of blood glucose (or blood sugar)[1]. The three types of Diabetes are; type I, type II and gestational diabetes.

Type 1 diabetes or insulin-dependent or juvenile diabetes occurs in any age but usually develops in children, teens, and young adults. Type 1 diabetes is thought to be caused by an autoimmune reaction that results in the self-destruction of beta-cells in the pancreas that produce insulin. This process can go on for months or years before the development of symptoms. It accounts for about 5-10% of Diabetes. Type 2 diabetes is characterized by variable degree of insulin resistance, impaired insulin secretion and increased glucose production. Gestational DM is a type of DM with hyperglycemia in pregnant women not diabetic prior to conception (usually starts at 13 week of gestation), and may disappear after delivery[2].

The prolonged hyperglycemia of diabetes leads to long-term health consequences which include cardiovascular, ocular, renal and neuronal complications[3]. Diabetes is a non-communicable disease and a leading cause of morbidity and mortality globally[1]. For example, it is estimated that impaired healing of diabetic wounds affects approximately 25% of all patients with diabetes mellitus, often resulting in lower limb amputation, with subsequent high economic and psychosocial costs. One estimate suggests that between one in three to one in every five patients with DM will develop a chronic non-healing wound in their lifetime, such as a diabetic foot ulcer (DFU), with an alarming recurrence rate (40% within one year and 65% within five years) and no reliable methods available to predict its occurrence[4 & 5].

About 422 million people worldwide have diabetes, the majority living in low-and middle-income countries, and 1.5 million deaths are directly attributed to diabetes each year[3]. The developing economies of Africa and Asia contribute a substantial fraction of this number. There is also a rising burden from the complications of DM alongside the ever-increasing prevalence of the disease[6]. In Nigeria, the current prevalence of DM among adults aged 20–69 years is reported to be 1.7%[7]. It is widely perceived that prevalence figures reported by the IDF grossly under-report the true burden of DM in Nigeria, given that they are derived through the extrapolation of data from other countries. Various researchers have reported prevalence ranging from 2% to 12% across the country in recent years[8].

This study aimed at utilizing Bayesian Survival Model to assessing the risk factors of type II diabetes among patients in two general hospitals in Nasarawa State, Nigeria. There are numerous risk factors for diabetes mellitus which can be classified into modifiable and non-modifiable risk factors. The modifiable factors are usually genetic factors and include age, sex, race/ethnicity and Body Mass Index (BMI). The non-modifiable risk factors include obesity, excessive alcohol intake, smoking, diets, sedentary lifestyle, hypertension, pregnancy, hypercholesterolemia, infections and polycystic ovarian syndrome[2].

Survival analysis is a set of statistical procedures utilized to analyze time to event data. It is a very valuable tool in clinical research and provides vital information for health intervention[8,9,10] applied the Kaplan Meire estimator and the Cox Proportional Hazard model to evaluate risk factors of DM. The results showed that old age, and risky behaviors (such as taking alcohol and smoking) are associated with higher death rates. Other risk factors are overweight, high blood pressure, and high cholesterol level[11] utilized Kaplan-Meier survival curves and Log-rank test in their study and opined that the survival times of patients among gender groups are different, with females being more likely to survive than as the males. In another study[12], found that male diabetics had an approximately equal survival as the females. They also found that married patients survived longer than unmarried/single patients[13] compared a class of Parametric and Semi-Parametric Survival Models fitted to Diabetic Data assuming various baseline distributions where results favored one of the Weibull AFT models. All of these authors employed similar survival tools in a frequentist approach and came to comparable conclusions[14] utilized a Bayesian Survival approach for estimating of the onset of time of nephropathy for patients with type II diabetic. In another form of model comparison[15] assessed the Classical and Bayesian Accelerated failure time model because of the failure in proportional hazard assumption fitted to diabetes mellitus data, the Bayesian Accelerated failure time model was seen in this case to be better than the Classical Accelerated failure time model with smaller AIC.

In this paper, the Bayesian frameworks employed the Weibull baseline for Proportional hazard (PH) & Accelerated Failure Time (AFT) models, for when variables are completely coded (categorical) and when some of the covariates are used in their metrical forms, to ascertain which of the model, best represent the records of patients managed for type II DM in Nasarawa West district, Nasarawa State, Nigeria and evaluate the measure of threat each of the risk factors considered in the study constitutes.

2.0 Materials and Method

Secondary data was obtained from the hospital records of 532 type II diabetes patients from two General hospitals in Nasarawa west district of Nasarawa State, Nigeria. The data obtained are the non-modifiable variables (age, gender) and modifiable variables-body mass index, systolic and diastolic blood pressures, drugs and location. The time from the diagnosis of the disease for in-patients to death defines the failure time while those whose records read "alive" were right-censored because such patients had not died as at the time of data collection.

2.0.1 Variable Transformation for coded model

For the sake of analysis, the covariate Age is categorized such that; age <40, serves as reference category and as such coded "0", age >=40 are coded "1". Gender was coded "1" for "male" patients and "0" for "female"

patients. BMI was coded "0" for "normal with BMI<=24.9", "1" for "low with BMI<=18.4" , "2" for "obese with BMI>24.9". Systolic Blood Pressure (SBP) was coded "0" for normal with SBP between "90-120" , "1" for low with SBP < 90", "2" for high with SBP >=140". Diastolic Blood pressure (DBP) was coded "0" for normal with DBP between "60-80" , "1" for low with DBP < 60", "2" for high with DBP >=90". Drugs critical for diabetic patients like (metformin and ACT) were coded "2", Glibendemid was coded "1" while others; for pain relief, Meloxicam drug for anti-inflammatory, malaria treatment drugs, Lishopril drug for hypertension, "no drugs cases" were all coded "0". For Location covariate or the spatial variable General Hospital Nasarawa (GHN) was coded "0" and made reference category, while General Hospital Keffi was coded "1".

For the outcome variable patients that experienced the event death were coded "1" while those that were alive as at the time of study or those that were discharged were considered to be right censored and coded "0".

2.0.2 Covariate representation in model when some covariates are not coded

Here, the variables Age, BMI, SBP, DBP are left in their metrical form with few unchangeable nominal covariates included in the model.

2.1 Methodology

In the analysis of survival data, models are classified into two board classes – the proportional hazard (PH) model and the Accelerated Failure rate (AFT) model. The proportional hazard model or the Constant Hazard (CH) model has been widely used and modified to accommodate several situations under the popular constant or proportional hazard postulation where in most cases the baseline distributions are either not specified or mildly done, and covariates are considered to have a multiplicative outcome on the hazard function. However, the AFT models in some situations become tenable when this assumption fails and in other situations when it presents a better performing model in comparison to the PH model, according to[16], Accelerated failure time (AFT) models are regression models for location – scale families, they represent a multiplicative rescaling of baseline time to event - they specifies that the covariates act multiplicatively on the failure times or additively on the log of the failure time.

2.2 Model Specification for PH and AFT

2.2.1 The PH model

$$\lambda_i(t,X) = \lambda_0(t)\exp.\left(\sum_{j=1}^{p}\beta_i X_i\right) \quad (1)$$

where $\lambda_0(t)$ is called the baseline hazard function, which is the hazard function for an individual for whom all the variables included in the model are zero, $X = (x_1, x_2 \ldots, x_p)'$ is the values of the vector of explanatory variables for a particular individual, and $\beta' = (\beta_1, \beta_2 \ldots, \beta_p)$ is a vector of regression coefficients.

2.2.2 The AFT model

$$T_i = \exp(Z_i\beta).\exp(\varepsilon_i) = \exp(Z_i\beta).T_{i0} \quad (2)$$

$T_{i0} = \exp(\varepsilon_i)$ – the baseline times

$\exp(\gamma' Z_i)$ represent the multiplicative rescaling of the baseline time (normal time), i.e. suppose $\exp(\gamma' Z_i) = 2$, it means that the

survival time T_i is going to be twice the normal time[16].

2.3 Models written in the functional covariate forms is

$$\eta(t;X_i) = f_0(t) + \sum_{i=1}^{p} f_i X_i \quad (3)$$

$$T(t;Z_i) = g_0(t) + \sum_{i=1}^{p} f_i Z_i \quad (4)$$

The function $f_0(t) = \delta \; and \; g_0(t)$ are log baseline effects for the PH and AFT models, and a function, $f_j(X_i) \; and \; f_j(Z_i)$ represent the general functional forms of covariate effects $x_i and \; z_i$ for PH and AFT respectively.

2.4 Model Likelihood for the modified PH and AFT models

$$L(t;\lambda,X_1) = \prod_{i=1}^{n} \exp(\lambda_0 \exp(X_i\beta)).\lambda_0 \exp(\exp(X_i\beta))^{d_i} \quad (5)$$

$$L(t;T,X_1) = \prod_{i=1}^{n} \exp(T_{i0} \exp(Z_i\beta)).T_{i0} \exp(\exp(Z_i\beta))^{d_i}. \quad (6)$$

The first part (exponential function) of the likelihood function of both the PH and AFT models are the contributions of those that survived in the study (censored event). While the second exponential function with the power d_i represents the contribution of the hazard function – subjects that experienced the event of interest.

2.5 PH and AFT models with regularized effects:

$$\begin{cases} \eta = B_0^T\omega + X_{1i}B_0^T\beta_i + X_{2i}\gamma_i \\ T_i = B_0^T\delta + Z_{1i}B_0^T\beta_i + Z_{2i}\gamma_i \\ (\omega|\tau^2) \sim RW(\tau^2, P_d);\; \tau^2 \sim \pi_{\tau^2} \\ (\delta|\tau^2) \sim RW(\tau^2, P_d);\; \tau^2 \sim \pi_{\tau^2} \\ \gamma \sim \pi \\ \left(\beta_i|\tau_j^2\right) \sim RW\left(\tau_i^2, P_d^{(i)}\right);\; \tau_i^2 \sim \pi_{\tau^2 i};\; i = 1,\dots,p \end{cases} \quad (7)$$

$\eta \; and \; T_i$ depicts the PH and the AFT models in additive forms, The continuous effects of metrical covariates for both models are given by $X_{1i}B_0^T\beta_i \; and \; Z_{1i}B_0^T\beta_i$ while $X_{2i}\gamma_i \; and \; Z_{2i}\gamma_i$ represents the categorical parts for both PH and AFT models respectively. The baseline functions and the metrical covariates for both models are implemented by random work priors and a noninformative prior π for the categorical covariates. τ^2 is the smoothing parameter, P_d is the penalized term of order d for the random walk process. πβ and π_{τ^2} are generic prior densities for the regression coefficients[17].

2.6 PH and AFT Model specification for analysis of diabetic dataset

This section models the diabetic data in as; Diabetic Additive Models – DAMS and this is represented in two forms;

i. Diabetic Additive Constant Hazard Model – DACHM
ii. Diabetic Additive Accelerated Failure Time Model – DAAFTM

$$\eta_{\text{DACHM}} = f_0(t) + AGE\beta_1 + BMI\beta_2 + SBP\beta_3 + DBP\beta_4 + DRUG\gamma_1 + GENDER\gamma_2 + SEX\gamma_3 + LOCATION\gamma_4 \quad (8)$$

$$\eta_{C.\text{DACHM}} = f_0(t) + AGE\gamma_1 + BMI\gamma_2 + SBP\gamma_3 + DBP\gamma_4 + DRUG\gamma_5 + GENDER\gamma_6 + SEX\gamma_7 + LOCATION\gamma_8 \quad (9)$$

$$T_{\text{DAAFTM}} = g_0(t) + AGE\beta_1 + BMI\beta_2 + SBP\beta_3 + DBP\beta_4 + DRUG\gamma_1 + GENDER\gamma_2 + SEX\gamma_3 + LOCATION\gamma_4 \quad (10)$$

Where; $f_0(t)$ is the Weibull baseline hazard function for PH model, $g_0(t)$ is the Weibull baseline time function for the AFT model, β_i are effects of metrical covariates, γ_i are effects of categorical covariates.

3.0 Results

Table 1: Summary table of some covariates

DAYS		AGE		W.KG.		H.M.	
Min.	: 5.0	Min.	: 29.00	Min.	: 37.00	Min.	: 1.560
1st Qu.	: 48.0	1st Qu.	: 53.00	1st Qu.	: 56.00	1st Qu.	: 1.700
Median	: 70.0	Median	: 60.00	Median	: 61.00	Median	: 1.760
Mean	: 101.7	Mean	: 60.78	Mean	: 61.34	Mean	: 2.437
3rd Qu.	: 106.0	3rd Qu.	: 69.00	3rd Qu.	: 67.00	3rd Qu.	: 1.830
Max.	: 341.0	Max.	: 98.00	Max.	: 97.00	Max.	: 185.000
			NA's:1				
BMI		SYSTOLIC		DIASTOLIC		CAGE	
Min.	: 0.0	Min.	: 60.0	Min.	: 40.00	Min.	: 0.0000
1st Qu.	: 17.3	1st Qu.	: 130.0	1st Qu.	: 60.00	1st Qu.	: 1.0000
Median	: 19.6	Median	: 150.0	Median	: 70.00	Median	: 1.0000
Mean	: 19.7	Mean	: 146.7	Mean	: 73.18	Mean	: 0.9196
3rd Qu.	: 21.8	3rd Qu.	: 170.0	3rd Qu.	: 90.00	3rd Qu.	: 1.0000
Max.	: 34.4	Max.	: 200.0	Max.	: 170.00	Max.	: 1.0000

Table 2: Test for Proportional hazard assumption for the diabetic data set when all covariates are coded

Metrical covariates not Categorized			Metrical variables Categorized	
Covariates	Chisq	p-value	Chisq	p-value
Age	2.3128	0.1238	0.0103	0.9192
BMI	0.1126	0.7372	0.5252	0.7691
CDT	0.2157	0.6423	0.4175	0.5182
CTYPE	9.6139	**0.0019**	8.3333	**0.0039**
CCOM	2.7526	0.0971	2.8846	0.0894
DRUGS	0.2157	0.8978	0.4175	0.8116
Systolic BP	0.1748	0.6759	3.1044	0.2118
Diastolic BP	0.7681	0.3808	6.3950	**0.0409**
Gender	0.0636	0.8008	0.0218	0.8826
Location	0.2671	0.1354	0.0582	0.8093
Global Test	16.1560	0.2490	20.5071	0.1149

Interpretation

It is observed from table 2; that covariates TYPE fails the constant hazard postulation with p-values, less than the significance level of 0.05 on both sides of the table while Diastolic Blood Pressure (DBP) fails when all

covariates were coded, which implies that hazard ratios are not constant for these covariates through the period of study. The global test however satisfies the constant hazard assumption.

Table 3: Model selection criteria for the Models

MODEL	WAIC	DIC	LPML
DACH	522.8674	5210141	-261.555
C.DACH	**521.4003**	**519.8032**	**-260.7888**
DAAFT	524.9087	522.7002	-262.5098

Interpretation

From table 3, it is clearly seen, that the PH models outperformed the AFT model with C. DAACH doing best in comparison to others, occasioned by least values of WAIC, DIC, which puts the model ahead in precision and a large LPML, allowing for a better predictive power for the model.

Table 4: Posterior coefficients for coded version of Diabetic Additive Constant Hazard Model

C.DACH		n=532	
Covariates		$\hat{\beta}$	Hazard ratios
AGE	$\hat{\gamma}_1$	-0.194	**0.82**
BMI	$\hat{\gamma}_2$	0.227	1.25
	$\hat{\gamma}_{21}$	-37.455	5.41E-17
SBP	$\hat{\gamma}_3$	2.107	8.23
	$\hat{\gamma}_{31}$	0.411	1.51
DBP	$\hat{\gamma}_4$	0.875	2.40
	$\hat{\gamma}_{41}$	1.971	7.18
DRUGS1	$\hat{\gamma}_5$	32.766	1.69886E+14
DRUGS2	$\hat{\gamma}_{51}$	32.310	**1.07611E+14**
GENDER	$\hat{\gamma}_6$	0.247	**1.28**
LOCATION	$\hat{\gamma}_7$	0.0158	**1.02**

Interpretation

Age covariate has a mean participation of 60.78 years, a coefficient of -0.19379, when exponentiated has a hazard ratio of 0.82, which implies that, those greater than 40 years of age with diabetes are most often and better managed for type II diabetics to avoid the hazard of death, as of the time of data collection. This age constitutes the most of the data as noticed with the mean age participation.

The BMI factor 1 covariate has a coefficient of 0.227, when exponentiated has a hazard ratio

of 1.25, which implies that those with BMI less than or equal to 18.4 (underweight) are 1.25 times at risk of death from diabetes than those of normal weight (between 18.4 – 24.9). BMI factor 2 covariate has a coefficient of -37.455, when exponentiated has a hazard ratio of 5.41E-17, which implies that those with BMI greater than 24.9 (overweight) are 5.41E-17 times at risk of death from diabetes than those of normal weight.

The SBP factor 1 covariate has a coefficient of 2.170, when exponentiated has a hazard ratio of 8.23, which implies that those with SBP less than 90 (low) are 8.23 times at risk of death from diabetes than those of normal SBP observed between (90 – 120)MMHg. SBP factor 2 covariate has a coefficient of 0.411, when exponentiated has a hazard ratio of 1.51, which implies that those with SBP greater to than 140 (high) are 1.51 times at risk of death from diabetes than those of normal SBP.

The DBP factor 1 covariate has a coefficient of 0.875, when exponentiated has a hazard ratio of 2.40, which implies that those with low DBP (DBP < 60) are 2.40 times at risk of death from diabetes than those of normal DBP (between 60 – 80). DBP factor 2 covariate has a coefficient of 1.971, when exponentiated has a hazard ratio of 7.18, which implies that those with DBP greater than or equal to 90 (high) are 7.81 times at risk of death from diabetes than those of normal DBP.

Patients that where place on drugs critical for type II diabetes (like, metformin, ACT and Glibendemid) were seen to be further at risk of death than patients on pain relief medication.

Gender covariate has a coefficient of 0.247, when exponentiated has a hazard ratio of 1.28, which suggest that male patients are 1.28 times at risk of death from diabetes than their female counterparts.

Location covariate or the spatial variable has a coefficient 0.0158 with the hazard ratio of 1.02, which suggests that patients at the General Hospital Keffi experience are 1.02 times at risk of death than those of the General Hospital Nasarawa.

3.1 Discussion

From the study, diabetes type II patients aged above 40 years had a lower risk of death than other ages. This is possibly because at the age, patients were mostly affected and managed in the hospitals. The drug therapy probably improved their health and reduced the risk of dying from the disease. This is probably the reason why the finding contrasts with that of[9,10] who found that old age is associated with a high risk of dying from diabetes.

The study found that Body Mass Index, BMI greater than 24.9 (overweight) are 5.41E-17 times at risk of death from diabetes than those of normal weight. This is because high BMI in diabetics is associated with poor glucose control.

Systolic Blood Pressure (SBP) is the pressure in the arteries when the heart beats. The study found that diabetic patients with high Systolic Blood Pressure (SBP), greater than 140 (high) increases the risk of dying from the diseases by 1.51 times than those of normal SBP. It also found that high Diastolic Blood Pressure, DBP, greater than or equal to 90 (high)

increases the risk of dying from the diseases by 7.81 times than those of normal DBP. High systolic and diastolic pressures are comorbidities of diabetes and have been found to worsen the clinical outcome of diabetes, These findings are similar to those of [8,9,10].

Male diabetic patient were 1.28 times at risk of death from diabetes than their female patients. This is similar to the findings of[11] who found that the survival times of patients among gender groups are different, with females being more likely to survive than as the males. However, the finding contrasts that of[12], who found that male diabetics had an approximately equal survival as the females.

The study found that the use of anti-diabetic drugs (Metformin and Glibendemid) were found to be at higher risk of death than patients on pain relief medication. This underscores the importance of the anti-diabetic drug therapy in the appropriate management of the disease to improve the quality of patients' life.

The patients' location was found to affect the survival of the patient to diabetes. Patients of General Hospital Keffi experience are 1.02 times at risk of death than those of the General Hospital Nasarawa. The slight difference may be due to variances in the quality of the health services in the two hospital facilities.

4.0 Conclusion

Bayesian Survival Model was successfully utilized to analyze the risk factors of Type II diabetes in the facilities studied. It found that, diabetes type II patients aged above 40 years had a lower risk of death than other ages. It found that the diabetic type II patients with high systolic pressures and those with high diastolic blood pressures were more likely to die from the disease than those with normal blood pressures. It also found that male patients were more likely to die than female patients. It found out that the patients on anti-diabetic drug therapy were more likely to die from the disease than those not on the drugs.

4.1 Recommendation

The research recommends that type II diabetes patients should:

1. comply with the drugs prescribed them.
2. maintain a healthy weight for example through routine physical exercise
3. monitor blood pressure regularly and maintain a healthy blood pressure.

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