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The Empirical Bayes of Occurrence of the Apnea among Sleep Apnea Patients

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Abstract: The prevalence of sleep apnea problem have rise since twenty years ago. Sleep apnea disrupts the quality of sleep and may influence quality of life. The purpose of this study was to find relationship between occurrence of apnea and occurrence of rapid eye movement (REm) sleep stages. The empirical Bayes method was used to estimates the rates of apnea and rates of REm among 13 patients that were suffering of sleep apnea problem. The data was extracted from PhysioBank website that consists of apnea events and sleep stages. In this study, The parameter estimates of Poisson-gamma model was considered. The estimation of parameter was done using three method which is moment (mom), maximum likelihood (mLE) and alternate method (mLM). The results indicated that the estimates of parameter was almost similar between three methods. The estimates of rates of apnea was not related to rates of REm. The rates of apnea and rates of REm was differed between the 1st and 2nd half period of sleep. Furthermore, there was no relationship between apnea and sleep stages of REm when the time of sleep was partition into 1st and 2nd period of sleep. Based on the bootstrapping method the estimates of parameter was found to be acceptable for a particular patients.

Key words: Apnea, REm, Poisson-gamma, bootstrapping

INTRODUCTION

Sleep apnea is one of the sleep disorder during sleep. The prevalence of apnea have risen especially among adults. Apnea may influence the quality of life of the patients as during the day the patients may have excessive daytime sleepiness. Previous study indicated that apnea was associated with hypertension and obesity (Katz, 1981; Nieto *et al*., 2004). Apnea can be categorized into Obstructive Sleep Apnea (OSA), Mixed Apnea (MA) and Central Apnea (CA). However, most cases of apnea was OSA. OSA is a presence of blockade in their throat during their sleep. The blockade caused a complete or partial cessation of airflow during the sleep contributing to a pause in breathing for at least 10 sec. Apnea may occur many time during sleep (Stradling and Davies, 2004.).

Sleep stages consists of awake, light sleep, deep sleep and Rapid Eye Movement (REm). Dreams usually occurred during REm. Sleep stages awake, light sleep and deep sleep was also known as non-REm (NREm) sleep stages. Previous study indicated that apnea was more serious during sleep stages REm compared to sleep stages non-REm (Trinder *et al*., 2001). A study by Findley *et al*. (1985) among 12 patients of obstructive sleep apnea, showed that the duration of apnea was higher during sleep stages REm. Apnea Hypopnea Index (AHI) is a measurement to classify the severity of apnea. AHI was calculated base on the total apnea per hour. Then the AHI was categorized into groups. AHI was used to describe the prevalence of apnea in most research regarding apnea. For example study by Duran *et al*. (2001), indicating that the prevalence of apnea in population was 4% among men and 3% among women that have AHI at least 10. However, as studied by Bixler *et al*. (1998) the prevalence of apnea was 3% in population that has AHI more than 10 and related to Excessive Daytime Sleepiness (EDS).

Empirical Bayes (EB) method has been used in many areas such as medical and environment. In Bayesian, it allows the researcher to use a distribution that was belief to be suitable for a particular data. The distribution was called prior distribution (Suggs and Curran, 1983). For example for incidence rate and relative risk, the prior distribution was gamma. Some studies has showed that empirical bayes approach is particularly suitable to select the hyperparameter for incidence rate and relative risk. Ogata *et al*. (2000) used the EB approach to

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analyse the incidence rate of diabetes with age and period of time. Clayton and Kaldor (1987) considered EB to find the difference between district for the standardized mortality rates of lip cancer in Scotland. In this study data was extracted from PhysioBank website (Goldberger *et al*., 2000), will be analyzed using empirical bayes for Poisson-gamma model. The objective of the study was to determine relationship between apnea rates and REm rates. Secondly to determine the difference of parameter estimates using methods moment (mom), maximum likelihood (mLE) and combination of moment and mLE (mLM).

MATERIALS AND METHODS

Suppose there was M apnea patients. The number of apnea for i patients is O_i and the total epoch of sleeping period was N_i with i = 1, 2, 3, ..., M. Assume that the rate of occurrence of apnea for every patients was equal, the expected number of occurrence of apnea for patients i was:

$$J_i = N_i(\sum_{i=1}^{M} O_i / N_i)$$

Suppose that the rate of occurrence of apnea for patients i was θ_i . The rate of occurrence of apnea was unknown. The estimate of maximum likelihood for the Rate of Apnea (RA) was given by:

$$\hat{\theta}_i = \frac{O_i}{J_i} = \frac{\text{No. of apnea (epoch)}}{\text{Total period of apnea (epoch)}}$$

Assume that the number of occurrence of apnea for patients i, O_i was a random variable from Poisson with the probability function:

$$f(O_i \mid \theta_i) = \frac{\exp(-J_i\theta_i)(J_i\theta_i)^{O}_i}{O_i!}$$

In Bayesian the likelihood was combined with the prior distribution, to find the posterior distribution. The conjugate prior for the Poisson distribution was gamma distribution. The marginal distribution was given by:

$$m(O_i \mid \alpha, v) = \frac{\Gamma(O_i + v)}{\Gamma(v)\Gamma(O_i + 1)} (\frac{\alpha}{J_i + \alpha})^{v} (\frac{J_i}{J_i + \alpha})^{O_i}$$

Based on the O_i that is known to estimate θ_i, the posterior distribution was given by:

$$p(\theta_i \mid O_i) = \frac{1}{\Gamma(O_i) + v} (J_i + \alpha)^{O_i + v} \exp[-(J_i + \alpha)^{\theta_i}]$$

$p(\theta_i \mid O_i)$ was distributed as gamma distribution with scale $J_i+\alpha$ and shape O_i+v parameter . The estimated mean was given by:

$$E(\theta_i \mid O_i) = \frac{O_i + v}{J_i + \alpha} = \theta^{ab}$$

The value of α and v would be estimate by three methods which is moment, maximum likelihood and combination of moment and maximum likelihood (Meza, 2003).

Moment method (mom): In order to use the moment method, the estimate of θ was given by:

$$\bar{\theta} = \sum wi\hat{\theta}_i$$
$$w_i = J_i / J_T$$

$$\hat{\theta}_i = O_i / J_i$$
$$J_T = \sum J_j$$

Using the θ_i, the parameter α and v can be estimate using:

$$\bar{\theta} = \sum wi\hat{\theta}_i$$

$$\alpha = \frac{\bar{\theta}}{\sum w_i (\widehat{\theta_i} - \bar{\theta_i})^2}$$

The parameter v was estimated using:

$$v = \frac{\bar{\theta}^2}{\sum w_i (\widehat{\theta_i} - \sum w_i \widehat{\theta_i})^2}$$

Maximum likelihood estimation (mLE): O_i was a negative binomial distribution with density function given by:

$$m(O_i \mid \alpha, v) = \frac{\Gamma(O_i + v)}{\Gamma(O_i + \alpha)\Gamma(v)} (\frac{\alpha}{J_i + \alpha})^{v} (\frac{J_i}{J_i + \alpha})^{O_i}$$

The log-likelihood was given by:

$$l(O_i) = \sum[\log(\frac{\Gamma(O_i + v)}{\Gamma(O_i + \alpha)\Gamma(v)}) + O_i \log J_i + v\log\alpha - (O_i + v)\log(J_i + v)]$$

by solving $\frac{\delta l}{\delta v} = 0$ and $\frac{\delta l}{\delta \alpha} = 0$, α and v was estimated.

Combination of moment and maximum likelihood (mLM):

$$\theta_i = \frac{O_i + v}{J_i + \alpha}$$

$$\bar{\theta}_i = \frac{1}{M}\sum_{i=1}^{M}\frac{O_i + v}{J_i + \alpha}$$

θ_i can be estimated by giving the initial value for α and v. The estimation θ will be repeated until α and v converge.

Uncertainty: In order to explain the variation between three methods, Bootstrap method was used to estimate the sampling error and bias. The measurement of uncertainty for the estimates from the three methods was bootstrapping:

- **Step 1:** Generate random number for the data of occurrence of apnea until Z times, with O_i Poisson ($J_i \theta_i$)
- **Step 2:** Using method discussed earlier to estimate the scale and shape parameter α and v
- **Step 3:** Sort the estimated value $\alpha_1, ..., \alpha_z$ and $v_1, ..., v_z$ from minimum until maximum
- **Step 4:** Calculate the quartile for 2.5 and 97.5% of the α and v. If the true estimate of α and v lies within the range, meaning that the shape and scale parameter is robust

RESULTS

The data were analyse using the EB with a prior gamma. The bootstrapping measuring the uncertainty in the estimation. Table 1 also showed that the Standard Deviation (SD) of the relative risk of occurrence of apnea was range from 0.044 until 0.144. Mean while the SD from the moments method was range between 0.016 until 0.052. This indicates that the estimation from moment method is stable compared to relative risk because the range of SD is low in variability (Meza, 2003).

From Table 1 the results shows subjects 7 has the most frequent apnea according to mLM, mLE and mom. Table 1 shows that for gamma prior the apnea rates range from 0.16 to 0.78. Based on Table 1, the estimation of parameter rates of apnea using the gamma model indicated that there is small variation between the mom, mLE and mLM method. For example, the estimation from mom was almost similar with the apnea rates with the range between 0.16 to 0.78. The estimation of parameter from mLM, mLE and mom was almost similar. For example for patients 2, the estimation of rates of apnea of mLM, mLE and mom was 0.248, 0.246 and 0.246, respectively. According to Meza (2003) the estimation of the mom, mLE and mLM will be almost similar to the apnea rates if the sample size is high. However, Table 1 shows that all the estimates was almost similar despite the period of sleep. For example patient 1, has the shortest period of sleep which is 2 h and patient 7 has the longest period of sleep which is 6 h but the estimates of rates of apnea was almost similar for all method that has been used.

Table 1: Estimates of rate of apnea

				Gamma	Model			
Subject	O	RA	AHI	SD (RA)	mLM $\theta_{Alternate}$	mLE θ_{mLE}	mom θ_{mom}	SD (mom)
1	37	0.154	18.5	0.066	0.164	0.165	0.169	0.025
2	87	0.242	29	0.067	0.246	0.246	0.248	0.025
3	241	0.335	40.17	0.056	0.335	0.335	0.335	0.021
4	317	0.440	52.83	0.064	0.439	0.438	0.439	0.024
5	182	0.255	30.58	0.049	0.257	0.257	0.258	0.018
6	118	0.184	22.13	0.044	0.188	0.188	0.189	0.016
7	554	0.793	95.24	0.087	0.786	0.785	0.784	0.033
8	214	0.282	33.78	0.049	0.283	0.283	0.283	0.019
9	294	0.386	46.26	0.058	0.386	0.386	0.387	0.022
10	341	0.480	57.63	0.067	0.478	0.477	0.478	0.025
11	253	0.351	42.17	0.057	0.352	0.351	0.352	0.022
12	229	0.522	62.59	0.089	0.517	0.517	0.517	0.033
13	73	0.474	56.88	0.144	0.466	0.465	0.466	0.052

Table 2: Estimation of occurrence of REm rates

			Gamma	Model			
Subject	RR	SD (RR)	mLM θ_{mLM}	mLE θ_{mLE}	mom θ_{mom}	SD (mom)
1	0.058	0.209	0.061	0.061	0.060	0.011
2	0.236	0.339	0.227	0.227	0.225	0.030
3	0.103	0.166	0.102	0.102	0.101	0.011
4	0.032	0.093	0.034	0.034	0.033	0.007
5	0.052	0.117	0.053	0.052	0.052	0.008
6	0.016	0.066	0.018	0.017	0.018	0.006
7	0.143	0.191	0.142	0.141	0.141	0.013
8	0.042	0.102	0.043	0.042	0.043	0.007
9	0.042	0.109	0.043	0.043	0.043	0.007
10	0.044	0.172	0.045	0.045	0.044	0.012
11	0.109	0.102	0.109	0.109	0.108	0.007

The estimation of rates of REm was presented in Table 2. There was no REm sleep stages for patients 12 and 13. The highest rates of REm was patients 2. Patients 6 has the lowest rate of REm during sleep. The estimation of rates of REm was almost similar from the three method. For example for patient 2, the estimates of rates of REm was 0.227, 0.227 and 0.225 for method mLM, mLE and mom, respectively. Regarding the relationship between apnea and REm, there was no relationship. For example patients 7 has the highest rates of apnea and higher rates of REm. However, patients 2 has the highest rates of REm but low rates of apnea (Table 1, 2).

Bootstrap method has been used to test for the robustness of parameter α and v. Both parameter is

Table 3: Parameter estimation α and v and the confidence interval with Bootstrap for rates of apnea and REm sleep stages

Method estimation	Parameter	Estimation parameters	Lower limit	Upper limit
REm				
mom	α	6.78	4.51	8.23
	v	30.74	20.65	38.04
mLM	α	5.44	3.57	6.46
	v	24.13	15.83	29.11
mLE	α	6.27	4.72	7.89
	v	27.68	21.02	35.61
Apnea				
mom	α	6.28	5.36	8.61
	v	16.21	14.29	22.89
mLM	α	6.29	5.38	8.09
	v	16.32	13.84	21.03
mLE	α	5.45	4.72	6.93
	v	14.43	12.41	18.47

Table 4: The rate of apnea using the mLM methods for first and second period of sleep

	Apnea		REm	
Patients	1st half period of sleep	2nd half period of sleep	1st half period of sleep	2nd half period of sleep
1	0.17	0.82	0.030	1.530
2	0.73	0.52	1.130	5.330
3	1.13	0.52	3.260	0.370
4	1.57	0.55	0.009	0.840
5	1.01	0.21	1.900	0.012
6	0.68	0.23	0.010	0.014
7	1.57	2.66	0.009	0.420
8	0.76	0.70	1.130	2.830
9	0.96	1.05	0.008	1.112
10	0.87	1.73	1.450	0.120
11	0.79	1.07	1.990	1.460
12	1.09	1.68	1.460	0.020
13	0.97	1.53	0.042	0.056

estimated based on the equation with the EB. The result in Table 3 shows that the parameter estimation α and v within the range, indicated that the empirical Bayes method is robust. For example from Table 3, the parameter estimates of occurrence of apnea from mLE method was 6.29 and it is within the range of 5.38 and 8.09.

In order to study if the apnea and REm was higher during beginning or the end of sleep, the period of sleep was divided into two. The results in Table 4 indicated that the rate of apnea was highest in the 1st half period (beginning) and 2nd half period (end) of sleep for patients 7. Meanwhile for REm sleep stages the rate was high for patient 3 during the 1st half period of sleep. In the 2nd half period of sleep patient 2 has the highest REm. The results also show that the occurrence of apnea and REm varies during sleep. For example, for patients 4 apnea rates was high in 1st half however in the 2nd half period of sleep the rate of apnea was low which is 0.55.

DISCUSSION

The gamma model is compared using the mom, mLE and mom. EB method is used to model the rates of apnea among 13 apnea patients. EB has the advantage to explain the rate of severity of apnea for every minutes. The empirical Bayes estimate is usually non zero estimate and the estimate from EB will be near to the rates of apnea for patients that has longer period of sleep (Meza, 2003). All the estimates are non zero for 13 patients. The shortest period of sleep was patient 1. Furthermore if the expected count is large the EB estimates is almost similar with the rate of occurrence of apnea for example patient 7.

The method of moments estimates was suggested by Meza (2003) to be estimated using the bootstrap. From Table 3 the results indicated that the Gamma model is stable because the estimates is within the range. The estimates of v was slightly different between mLE , mLM and the mom give the highest estimate of α and v parameter.

Previous study used AHI and RDI to describe the severity of apnea, however many studies indicated that the measurement of severity is not standardized as different study indicating different level of severity of apnea, for example the prevalence of apnea that has AHI>15 (Qureshi and Ballard 2003; Duran *et al*., 2001) and some prevalence of AHI>10. (Bixler *et al*., 1998) However, this standardization can be minimize using the empirical Bayes method because it can rank the severity of apnea and describe the severity of apnea per minute. Therefore the medical practitioner have more choice or options to describe the apnea to patients. It seems that other covariates should be used to describe the severity of apnea such as gender, age and type of disease the patients have for example hypertension, smoking and obesity.

CONCLUSIONS

In conclusion, the EB that was applied using the three different method of estimation allows a better estimator compared to the rate of occurrence of apnea. In addition there was small variation of parameter estimate between the three estimation methods. Furthermore using the moment method the parameter estimate was nearest to rate of apnea.

REFERENCES

Bixler, E.O., A.N. Vgontzas, T.T. Have, K. Tyson and A. Kales, 1998. Effects of age on sleep apnea in men: I. Prevalence and severity. Am. J. Respir. Crit. Care Med., 157: 144-148.

Clayton, D. and J. Kaldor, 1987. Empirical bayes estimates of age-standardized relative risks for use in disease mapping. Biometrics, 43: 671-681.

Duran, J., S. Esnaola, R. Rubio and A. Iztueta, 2001. Obstructive sleep apnea-hypopnea and related clinical features in a population-based sample of subjects aged 30 to 70 yr. Am. J. Respir. Crit. Care Med., 163: 685-689.

Findley, L., M. Unverzagt, R. Guchu, M. Fabrizio, J. Buckner and P. Suratt, 1995. Vigilance and automobile accidents in patients with sleep apnea or narcolepsy. Chest, 108: 619-624.

Goldberger, A.L., L.A.N. Amaral, L. Glass, J.M. Hausdorff and P.C.H. Ivanov *et al*., 2000. PhysioBank, physioToolkit and physioNet: Components of a new research resource for complex physiologic signals. Circulation, 101: e215-e220.

Katz, R.W., 1981. On some criteria for estimating the order of Markov chain. Technometrics, 23: 243-249.

Meza, J.L., 2003. Empirical bayes estimation smoothing of relative risks in disease mapping. J. Stat. Plan. Inference, 112: 43-62.

Nieto, F.J., D.M. Herrington, S. Redline, E.J. Benjamin and J.A. Robbins, 2004. Sleep apnea and markers of vascular endothelial function in a large community sample of older adults. Am. J. Respir. Crit. Care Med., 169: 354-360.

Ogata, Y., K. Katsura, N. Keiding, C. Holst and A. Green, 2000. Empirical bayes age-period-cohort analysis of retrospective incidence data. Scand. J. Stat., 27: 415-432.

Qureshi, A. and R.D. Ballard, 2003. Obstructive sleep apnea. J. Allergy Clin. Immunol., 112: 643-651.

Stradling, J.R. and R.J. Davies, 2004. Sleep. 1: Obstructive sleep apnoea/hypopnoea syndrome: Definitions, epidemiology and natural history. Thorax, 59: 73-78.

Suggs, J.C. and T.C. Curran, 1983. An empirical Bayes method for comparing air pollution data to air quality standards. Atmospheric Environ., 17: 837-842.

Trinder, J., J. Kleiman, M. Carrington, S. Smith, S. Breen, M. Tan and Y. Kim, 2001. Autonomic activity during human sleep as function of time and sleep stages. J. Sleep Res., 10: 253-264.