**Reviewer’s Comments**

****

**COVID-19 KINETICS BASED ON REPORTED DAILY INCIDENCE IN HIGHLY DEVASTATED GEOGRAPHICAL REGION: A UNIQUE ANALYSIS APPROACH OF EPIDEMIC**

**Abstract**

**Keywords:** Control chart,correlation coefficient,COVID-19, exponential association,morbidity, mortality.

**Introduction**

The viral pandemic that has impacted the globe recently due to COVID-19 has affected the whole world at various levels and in different fields1. These devastating effects are the consequences of the catastrophic public health influence that hits the communities2. Two metrics are extensively and comprehensively used to measure the disease dynamic effect and pattern on the populations3. These measures are the reported cases and deaths based on the daily records by the official health organizations worldwide as could be also calculated on the cumulative basis.

In previous work, cumulative data records were analyzed following the Pareto principle showed that the USA is one of the major geographical areas influenced by morbidity and mortality cases with cumulative cases accounting for a fifth of the record and cumulative deaths of about 16.4%4. This analysis will make use of the same data source as in later research work5. The following investigation would demonstrate a new perspective quantitative examination using morbidities and mortalities as indicators by focusing on the USA case over long-term monitoring for more than two years and showing 0.7322 Spearman correlation (95%) at P<0.001 between new daily emerging cases and deaths.

Monitoring of daily reported cases and deaths over 743 days between 03 January 2020 and 14 January 2022 is shown as a three-dimensional relationship through two perspectives in Figure 1. The surface plot shows the side while the contour plot illustrates the top view showing the visual association between morbidity and mortality, confirming the correlation result. The 3D-chatting was segregated into 2D-trending graphs where Laney attribute charts were selected to provide an advantage to look into pattern and incident behavior6-8. There is an insight into six waves of morbidity cases associated with the same number of mortality incidents that follow the first chronologically after 42 days of the lag period (Figure 2). The process-behavior charts demonstrate observable excursions in count either high or low by red dots which might be due to excessive counts or potential shifting in the trend mean. Control charts show exploratory Upper Control Limit (UCL), Lower Control Limit and the average$(\overline{U})$. The mortality rate – expressed as percentage – from the total emerged cases has a lower limit of 1.04%, center value of 1.33% and upper boundary of 1.42%.

The proposed analysis herein provides an examination of the cumulative cases and deaths after the logarithmic transformation of data plus one (to compensate for zero values without distorting the dataset)9,10. The logarithmic transformation has shown previous improvements in reducing the scattering of the record points minimizing outliers and mitigating extreme values11. Figure 3 shows the correlation between the recorded cases and deaths of COVID-19 during the investigation period of the outbreak. There was a linear relationship with good regression and low standard error. The associated table shows the numerical analysis of the regression statistics. The threshold of the mortality count of zero reported deaths is one for emerging infection cases at the x-axis intercept. Residuals did not show systematic or fixed bias with the increasing number of the affected individuals.

Polynomial fitting was excluded from modeling where overfitting might occur due to response to excessive noise that occur normally in natural data that would complicate the outcome with multiple order polynomial that could be more than 10th order12.Study the kinetics of morbidity and mortality as daily cumulative numbers of the untransformed data showed Morgan Morgan and Finney(MMF) Model: *y=(a\*b+c\*x^d)/(b+x^d)* as a best fit with good correlation coefficient of 0.9870977 but high standard error of 2821207.2882689 when using the raw dataset of the reported cases as an example13, 14. The iteration count of 100 was exceeded.The fit failed to converge to tolerance of 0.000001 (CHI2 at 5881856606338862.000000) and no weighting was used according to report generated by software15. However, using the logarithmic transformation demonstrated reasonably low error value without significant decrease in the regression as could be seen in Figure 4.This transformation was favored in previous instances16. The modified results showed fitting to the exponential association: *y=a(1-exp(-bx)* for cases and *y=a(b-exp(-cx))*for deaths17-19. The fit converged to a tolerance of 1e-006 in 5 and 7 iterations and no weighting was used for morbidity and mortality, respectively20. Figure 5 demonstrates the difference between the residuals between both original (cases are only shown as an example) and the transformed data.

****

****

**Figure 1: Three-dimensionaltrend monitoring of the reported sickness cases and deaths attributed to COVID-19 over more than two years**





**Figure 2: Process-behavior chart of the Laney type showing the pattern of Coronavirus disease waves and magnitude in terms of morbidities and mortalities on daily basis over 743 days (red marks are indicative of aberrant numbers either high or low)**

|  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- |
| ***Regression Statistics*** | ***Statistics*** | ***df*** | ***SS*** | ***MS*** | ***F*** | ***Significance F*** |
| **Multiple R** | 0.9921 | **Regression** | 1 | 1991.267 | 1991.267 | 46543.14 | 0 |
| **R Square** | 0.9843 | **Residual** | 741 | 31.702 | 0.042783 |  |  |
| **Adjusted R Square** | 0.9843 | **Total** | 742 | 2022.969 |   |   |   |
| **Standard Error** | 0.2068 | **Regression equation:***y = 0.8526x - 0.607* |
| **Observations** | 743 |

**Figure 3: Correlation between reported cumulative daily cases and deaths after logarithmic transformation with the associated regression statistical analysis (C.C.: Cumulative Cases and C.D: Cumulative Deaths)**





**Figure 4: Modeling of daily cumulative morbidity cases (upper) and mortality cases (lower) of COVID-19 based on the logarithmic transformation showing the standard error of the regression (S) and correlation coefficient (r)**

**Figure 5: Residual analysis of raw (cases are shown here only as an example) and transformed data demonstration mitigation in the scattering in the values**

In this letter, a quantitative estimation of the outbreak magnitude and extent could be delivered comprehensively using simple and useful statistical techniques for the sake of public health safety in epidemic times. These fast tools could be used to aid in imposing measures by healthcare professionals, practitioners and officials by understanding the disease pattern and progression. With this regard, it could be concluded that there is a strong association between mortalities and morbidities of the COVID-19 illness, even when it could be observed that the mortality rate is very low – if compared with other catastrophic pandemics – over 24.4 months period. Data transformation improved points fitting with low errors and residuals with acceptable regression. Control charts showed signs of multiple overlapping outbreak waves with no signs of recession during the examination period. The exponential association model was the best fit for the cumulative data points of the count of the affected individuals in the morbidity and mortality. It describes the interaction between the population and the virus with elapsed time as a cumulative rate. This model could serve as a quantitative comparison tool for before and after actions to measure enhancement or deterioration, in addition to estimating variations between different geographical regions. From this proposal, this study could be extended to other countries, especially those with high priority in a series of investigational analyses to assess COVID-19 extension and level around the world to be prepared for the worst scenario of the next global pandemic with a risk of more casualties.

**ACKNOWLEDGMENTS:** None to declare.

**CONFLICT OF INTEREST:**No conflict of interest associated with this work.

**Author’s Contribution**

**REFERENCES**

1. Hiscott J, Alexandridi M, Muscolini M, Tassone E, Palermo E, Soultsioti M, Zevini A. The global impact of the coronavirus pandemic. Cytokine & growth factor reviews 2020; 53:1-9.*doi: 10.1016/j.cytogfr.2020.05.010*
2. Shadmi E, Chen Y, Dourado I, Faran-Perach I, Furler J, Hangoma P, Hanvoravongchai P, Obando C, Petrosyan V, Rao KD, Ruano AL. Health equity and COVID-19: global perspectives. International journal for equity in health. 2020;19(1):1-6.*https://doi.org/10.1186/s12939-020-01218-z*
3. MacKenzie DI, Nichols JD, Royle JA, Pollock KH, Bailey LL, Hines JE. Occupancy applications. Occupancy estimation and modeling. Elsevier Inc, Amsterdam. 2018.
4. Eissa ME, Rashed ER, Eissa DE. Implementation of the Pareto principle in focus group generation based on global coronavirus disease morbidity and mortality rates. Highlights in BioScience. 2022;5.*DOI:10.36462/H.BioSci.202204*
5. EİSSA M, Rashed ER, Eissa DE. Modeling of COVID-19 Major Outbreak Wave Through Statistical Software: Quantitative Risk Evaluation and Description Analysis. ESTÜDAM HalkSağlığıDergisi. 2022;7(1):145-61.[*https://doi.org/10.35232/estudamhsd.1024129*](https://doi.org/10.35232/estudamhsd.1024129)
6. Eissa M, Rashed ER, Eissa DE. Implementation of Modified Q-Control Chart in Monitoring of Inspection Characteristics with Finite Quantification Sensitivity Limits: A Case Study of Bioburden Enumeration in Capsule Shell. El-Cezeri. 2021; 8(3): 1093-1107.[*https://doi.org/10.31202/ecjse.871179*](https://doi.org/10.31202/ecjse.871179)
7. Mohammed MA, Panesar JS, Laney DB, Wilson R. Statistical process control charts for attribute data involving very large sample sizes: a review of problems and solutions. BMJ quality & safety. 2013;22(4):362-8.*http://dx.doi.org/10.1136/bmjqs-2012-001373*
8. Eissa ME. Variable and attribute control charts in trend analysis of active pharmaceutical components: Process efficiency monitoring and comparative study. Experimental Medicine (EM). 2018;1(1):32-44.*DOI: 10.31058/j.em.2018.11003*
9. Cheadle C, Vawter MP, Freed WJ, Becker KG. Analysis of microarray data using Z score transformation. The Journal of molecular diagnostics. 2003;5(2):73-81.[*https://doi.org/10.1016/S1525-1578(10)60455-2*](https://doi.org/10.1016/S1525-1578%2810%2960455-2)
10. Potamitis I, Fakotakis N, Kokkinakis G. Reliable ASR based on unreliable features. InASR2000-Automatic Speech Recognition: Challenges for the new Millenium ISCA Tutorial and Research Workshop (ITRW) 2000.
11. Kenkel NC. On selecting an appropriate multivariate analysis. Canadian Journal of Plant Science. 2006;86(3):663-76.*https://doi.org/10.4141/P05-164*
12. Royston P, Ambler G, Sauerbrei W. The use of fractional polynomials to model continuous risk variables in epidemiology. International journal of epidemiology. 1999;28(5):964-74.*https://doi.org/10.1093/ije/28.5.964*
13. Uba G, Yakasai HM, Abubakar A, Abd Shukor MY. Predictive Mathematical Modelling of the Total Number of COVID-19 Cases for Brazil. Journal of Environmental Microbiology and Toxicology. 2020;8(1):16-20.*https://doi.org/10.54987/jemat.v8i1.517*
14. Umar AM, Abd Shukor MY. Predictive Mathematical Modelling of the Total Number of COVID-19 Cases for Indonesia. Journal of Environmental Microbiology and Toxicology. 2020;8(1):27-31.*https://doi.org/10.54987/jemat.v8i1.519*
15. Baranenko AV. St. Petersburg State University of Low Temperature and Food Technologies: into the 21st century with new hopes. Refrigeration Technology. 2001;90(4):2-3.
16. Sivrikaya O, Tunç E. Demand forecasting for domestic air transportation in Turkey. The Open Transportation Journal. 2013;7(1).*DOI: 10.2174/1874447820130508001*
17. Jiménez-Díaz MB, Mulet T, Viera S, Gómez V, Garuti H, Ibáñez J, Alvarez-Doval A, Shultz LD, Martínez A, Gargallo-Viola D, Angulo-Barturen I. Improved murine model of malaria using *Plasmodium falciparum* competent strains and non-myelodepleted NOD-scid IL2R γ null mice engrafted with human erythrocytes. Antimicrobial agents and chemotherapy. 2009;53(10):4533-6.*https://doi.org/10.1371/journal.pone.0002252*
18. Khan J, Qi A, Khan MF. Fluctuations in number of *Cercosporabeticola* conidia in relationship to environment and disease severity in sugar beet. Phytopathology. 2009;99(7):796-801.*https://doi.org/10.1094/PHYTO-99-7-0796*
19. Juárez Tomás MS, Wiese B, Nader‐Macías ME. Effects of culture conditions on the growth and auto‐aggregation ability of vaginal *Lactobacillus johnsonii* CRL 1294. Journal of applied microbiology. 2005;99(6):1383-91.[*https://doi.org/10.1111/j.1365-2672.2005.02726.x*](https://doi.org/10.1111/j.1365-2672.2005.02726.x)
20. Saeed M, Jamal MA, Ilyas M, Younas M, Shahzad MA. Oxidative degradation of methylene blue in aqueous medium catalyzed by lab prepared nickel hydroxide. International Journal of Chemical Reactor Engineering. 2016;14(1):45-51.[*https://doi.org/10.1515/ijcre-2015-0088*](https://doi.org/10.1515/ijcre-2015-0088)