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Explaining Ovarian Cancer Data with Increasing Hazard Model

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Abstract: A single parameter model is developed in this study and used to understand ovarian cancer data. Its several mathematical and statistical properties such as the hazard rate function, moments, moment generating function, mean residual life function, renyi entropy, Bonferroni and Lorenz curve along with order statistics are derived. Maximum likelihood method is used to estimate the parameter. Also the importance of proposed model is checked for engineering data. Analysis reveals that the proposed model has potential to provide a better explanation than several existing lifetime models.

Keywords: Bonferroni and Lorenz curve, MRLF, Overian cancer, Renyi Entropy, MGF, K-S.

1 Introduction

Cancer starts when damage cells in the body begin to grow out of control in random direction. This can observe in any part of the body and spread further. Ovarian cancer is a type of cancer that begins in the ovaries of the female. The female reproductive system contains two ovaries, one on each side of the uterus. The disease typically presents in postmenopausal women i.e. is most common in women aged above 50 years, with a few months of abdominal pain and distension. In general, cancer begins when a cell develops mutations in its DNA. The mutations indicates the cell grow and multiply quickly, creating a tumor of abnormal cells. The stages of ovarian cancer ranges from stage 1 to stage 4, lower the number less the cancer has spread and continuously higher the number means the cancer has spread more. Surgery is the main treatment for most ovarian cancer and it depends on spread and health condition of the patients. The surgery is also done for the early stage and in advanced stage ovarian cancer. For more details about ovarian cancer see [1,2,3,4]. The risk of cancer is increasing with age is increasing. To understand its nature of survival pattern, a distribution of increasing type hazard may be suitable. Statistical distributions plays a vital role in describing and projecting the real life phenomenon.

A lot of mixture, extended, modified and generalized distributions have been extensively studied for modeling of real life problems and checked their suitability for various data sets. Many recent studies focused on deriving new distributions with the help of existing well-known distributions and increased their worth with adding flexibility in modeling data. Several distributions have been introduced by using a mixing approach. Lindley distribution, [5], is useful for analysing lifetime data, especially in stress-strength reliability modeling and hence provides gain over exponential and gamma distribution. [6] studied the properties of the one parameter Lindley distribution also applied it to waiting time data. A flexible continuous distribution proposed and compared with some competent various well known distributions for some real data sets [7]. Further, [8], [9], [10], [11], [12], [13] suggested some modified, extended, weighted and generalized form of distribution. In this study, a new distribution with increasing hazard is proposed which is more flexible for modeling lifetime data and utilize ovarian cancer data to check its suitability.

The propose distribution which is the mixture of gamma (2, θ) i.e. length biased exponential (θ) and gamma (3, θ) i.e. area biased exponential (θ) and thus named as mixture of length and area biased exponential distribution (mLAE).

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Now we have

$$f(x;\theta) = pf_1(x;\theta) + (1-p)f_2(x;\theta)$$

where

$$p = \frac{\theta}{\theta+2}, \quad f_1(x;\theta) = \theta^2 x.e^{-\theta x}, \quad f_2(x;\theta) = \frac{\theta^3}{2}x^2 e^{-\theta x}$$

Then the pdf of this one parameter proposed distribution with parameter (θ) is written as

$$f(x;\theta) = \frac{\theta^3}{\theta+2}e^{-\theta x}x(x+1); \quad x>0, \theta>0 \qquad (1)$$

The plot of probability density function of proposed distribution is given in figure (1)

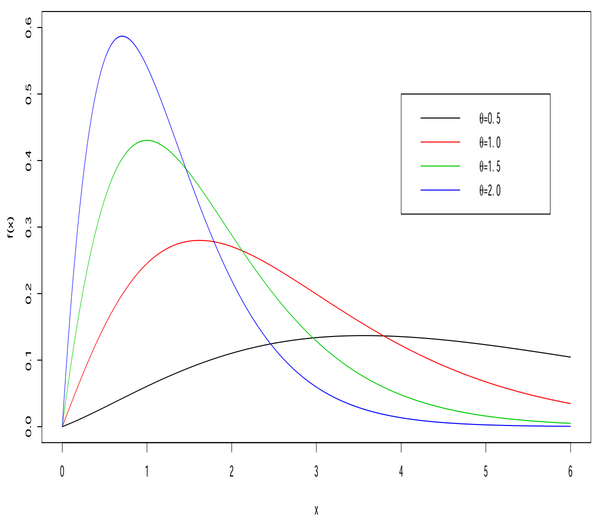

Fig. 1: Probability Density Function of mLAE

The cumulative distribution function for the proposed distribution can be written as

$$F(x) = \int_0^x f(t)dt = 1 - \frac{\left[\theta(1+\theta x) + (\theta^2 x^2 + 2\theta x + 2)\right] e^{-\theta x}}{\theta+2} \qquad (2)$$

The plot of cumulative distribution function of proposed distribution distribution is given in figure (2).

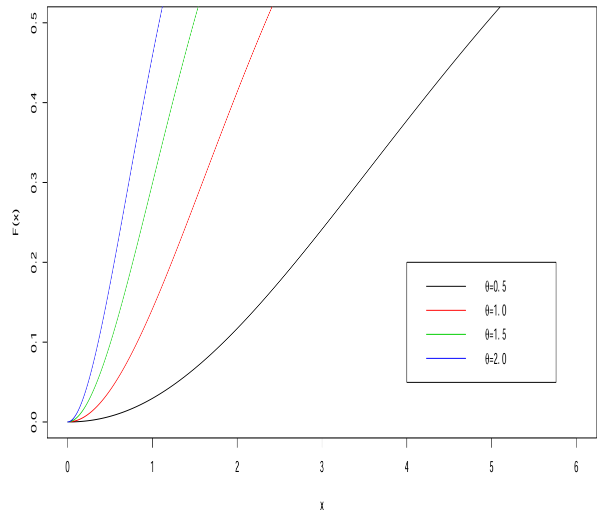

Fig. 2: Cumulative Distribution Function of mLAE

Let, $f(x)$ and $F(x)$ be the p.d.f. and c.d.f. of a continuous random variable. The hazard rate function (also known as the failure rate function), survival function and the mean residual life function of X are given in equation (3), (6) and (8) respectively as

$$h(x) = \frac{f(x)}{S(x)} = \frac{f(x)}{1-F(x)} = \frac{\frac{\theta^3}{\theta+2}e^{-\theta x}x(x+1)}{\frac{\left[\theta(1+\theta x)+(\theta^2x^2+2\theta x+2)\right]e^{-\theta x}}{\theta+2}}$$

$$h(x) = \frac{\theta^3\left(x+x^2\right)}{\theta(1+\theta x)+(\theta^2x^2+2\theta x+2)} \qquad (3)$$

Now, differentiating equation (3) with respect to x we get

$$h'(x) = \frac{\theta^3\left[\theta(1+2x+2x^2)+2(1+2x)\right]}{\left[\theta(1+\theta x)+(\theta^2x^2+2\theta x+2)\right]^2} \qquad (4)$$

Now as $x \longrightarrow 0$ we get

$$h'(0) = \frac{\theta^3}{\theta+2} > 0 \quad \forall \quad \theta > 0. \qquad (5)$$

Hence from (5) we can say that hazard is increasing i.e. the proposed distribution is of increasing hazard and the plot of hazard function is given in figure (3).

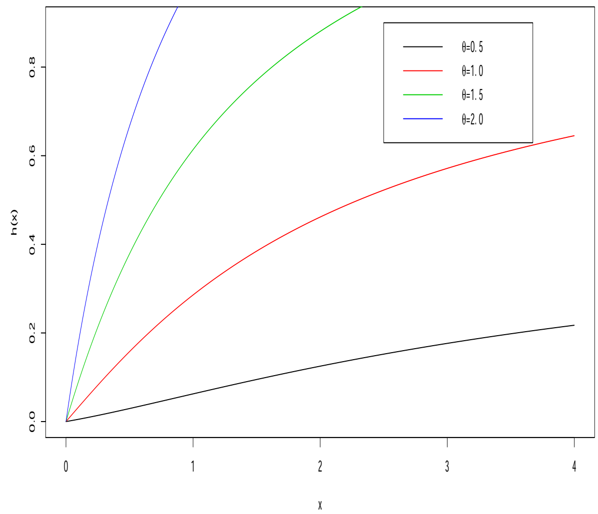

Fig. 3: Hazard Function of mLAE

The survival function of the proposed distribution is given as

$$S(x)=\int_x^\infty f(t)dt=1-F(x)$$
$$=\frac{\left[\theta(1+\theta x)+(\theta^2x^2+2\theta x+2)\right]e^{-\theta x}}{\theta+2} \qquad (6)$$

The plot of survival function is given in figure (4)

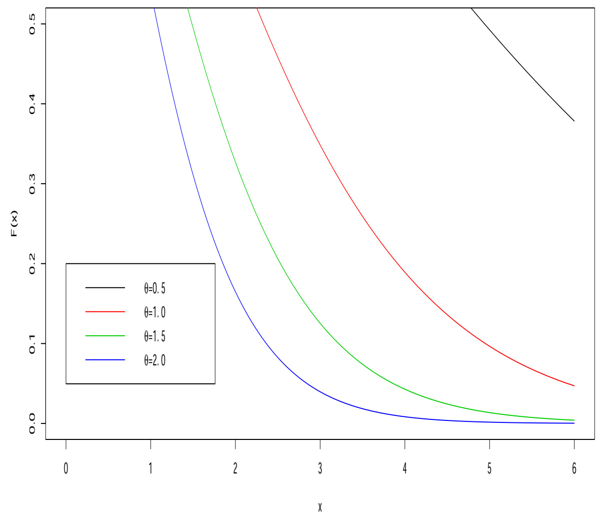

Fig. 4: Survival Function of mLAE

Mean residual life function for the proposed distribution can be given as

$$m(x)=E(X-x|X>x)=\frac{1}{S(x)}\int_x^\infty tf(t)dt-x$$
$$=\frac{1}{S(x)}\int_x^\infty t\frac{\theta^3}{\theta+2}e^{-\theta t}t(t+1)-x$$
$$=\frac{1}{S(x)}\frac{\theta^3}{\theta+2}\int_x^\infty te^{-\theta t}\left(t+t^2\right)-x$$
$$=\frac{1}{S(x)}\left(\frac{\theta^3}{\theta+2}\right)$$
$$\left[\frac{\left(\theta^2x^2+2\theta x+2\right)e^{-\theta x}}{\theta^3}+\frac{\theta^3x^3+3\theta^2x^2+6\theta x+6}{\theta^4}\right]-x \qquad (7)$$

After solving the above equation, we get,

$$m(x)=\frac{\left[\theta\left(\theta^2x^2+2\theta x+2\right)+\left(\theta^3x^3+3\theta^2x^2+6\theta x+6\right)\right]}{\theta\left[\theta(1+\theta x)+\left(\theta^2x^2+2\theta x+2\right)\right]}-x \qquad (8)$$

Now, if we put $x=0$, i.e $m(0)$ in (8), we get mean of the distribution $m(0)=\frac{2(\theta+3)}{\theta(\theta+2)}$.
Also reverse hazard function mLAE are given as,

$$\tau=\frac{f(x;\theta)}{F(x;\theta)}=\frac{\theta^3(x^2+x)e^{-\theta x}}{(\theta+2)-[(1+\theta x)(\theta+1+\theta x)+1]e^{-\theta x}} \qquad (9)$$

If we want to know the quartile, deciles and percentiles scores then quantile function is required. The inverse of the cumulative distribution function is known as quantile function and tells us what x would make $F(x)$ return the value p. Every cumulative distribution function has not a closed form inverse, therefore in such cases the inverses can be found using numerical methods.

The quantile function for *mLAE* distribution is defined in the form $x_q=u=F^{-1}(q)$ where u is the quantile function of $F(x)$ over the range $u\in(0,1)$. If $X\sim mLAE(\theta)$, then quantile function of X is the solution of the equation (10).

$$(1-u)(\theta+2)=\left[\theta(1+\theta x)+\left(\theta^2x^2+2\theta x+2\right)\right]e^{-\theta x} \qquad (10)$$

2 Statistical properties and Related measures

2.1 Moments, Moment generating function and Characteristics function

The moment generating function characterizes the distribution whereas moments are important in any statistical analysis, especially in applications on data. One can also obtain moments with the help of moment generating function. The most important features and characteristics of a distribution (e.g. central tendency, dispersion, skewness, and kurtosis) can be easily studied with the help of moments.

The r-th moment about origin of the proposed distribution is given by:

$$\mu_r' = E(X^r) = \int_0^\infty x^r f(x)dx$$

so that

$$\mu_r' = \frac{\Gamma(r+2)(\theta+r+2)}{\theta^r(\theta+2)} \tag{11}$$

Now, putting $r = 1,2,3\ldots$ we get the first four moments aspects

$$\mu_1' = E(X) = \frac{2(\theta+3)}{\theta(\theta+2)}$$

$$\mu_2' = E(X^2) = \frac{6(\theta+4)}{\theta^2(\theta+2)}$$

$$\mu_3' = E(X^3) = \frac{24(\theta+5)}{\theta^3(\theta+2)}$$

$$\mu_4' = E(X^4) = \frac{120(\theta+6)}{\theta^4(\theta+2)}$$

therefore,

$$V(x) = \mu_2' - (\mu_1')^2 = \frac{2(\theta^2+6\theta+6)}{\theta^2(\theta+2)^2} \tag{12}$$

now, the moment generating function and characteristic function are derived. The moment generating function is given by the relation

$$M_x(t) = \int_0^\infty e^{tx} f(x)dx$$

then, we have,

$$M_x(t) = \int_0^\infty e^{tx} \frac{\theta^3}{\theta+2} e^{-\theta x} x(x+1)dx$$

After solving the above equation, we get,

$$M_x(t) = \frac{\theta^3}{\theta+2}\left[\frac{(\theta-t)+2}{(\theta-t)^3}\right] \tag{13}$$

now, replacing it for t in equation (13), we get the corresponding Characteristics function for the proposed distribution that can be written as in equation (14).

$$\phi_x(t) = \frac{\theta^3}{\theta+2}\left[\frac{(\theta-it)+2}{(\theta-it)^3}\right] \tag{14}$$

2.2 Rényi Entropy

Entropy is a measure of the uncertainty associated with a random variable. The Rényi entropy is nothing but a useful generalization of Shannon entropy. It is also important in quantum information, where it can beused as a measure of entanglement; e.g. see [14], [15].
The Rényi entropy of the proposed distribution is given as

$$T_R(\eta) = \frac{1}{1-\eta}\log\int_0^\infty f^\eta(x)dx$$

$$T_R(\eta) = \frac{1}{1-\eta}\log\left[\frac{\theta^{3\eta}}{(\theta+2)^\eta}\right]\int_0^\infty \left[e^{-\eta\theta x}x^\eta(1+x)^\eta\right]dx$$

Now, using binomial expansion $(1+x)^n = \sum_{k=0}^{n}\binom{n}{k}x^k$ in above equation, we get,

$$T_R(\eta) = \frac{1}{1-\eta}\log\left[\frac{\theta^{3\eta}}{(\theta+2)^\eta}\sum_{k=0}^{\eta}\binom{\eta}{k}\frac{\Gamma(\eta+\theta+1)}{(\eta\theta)^{\eta+\theta+1}}\right] \tag{15}$$

2.3 Bonferroni and Lorenz curves

The Bonferroni and Lorenz curves see, [16] and Bonferroni and Gini indices have applications not only in economics to study inequality of income and poverty, but also in other fields like reliability, demography, insurance and medicine. The Bonferroni curve $B(p)$ and Lorenz curves $L(p)$ are defined as

$$\begin{aligned} B(p) = \frac{1}{p\mu}\int_0^q xf(x)dx &= \frac{1}{p\mu}\left[\int_0^\infty xf(x)dx - \int_q^\infty xf(x)dx\right] \\ &= \frac{1}{p\mu}\left[\mu - \int_q^\infty xf(x)dx\right] \end{aligned} \tag{16}$$

and

$$\begin{aligned} L(p) = \frac{1}{\mu}\int_0^q xf(x)dx &= \frac{1}{\mu}\left[\int_0^\infty xf(x)dx - \int_q^\infty xf(x)dx\right] \\ &= \frac{1}{\mu}\left[\mu - \int_q^\infty xf(x)dx\right] \end{aligned} \tag{17}$$

Using the proposed pdf, we get,

$$\int_q^\infty xf(x)dx = \left[\frac{\theta\left(\theta^2q^2+2\theta q+2\right)+\left(\theta^3q^3+3\theta^2q^2+6\theta q+6\right)}{\theta+2}\right]e^{-\theta q} \tag{18}$$

So, from the above equations, we get,

$$B(p) = \frac{1}{p}\left[1 - \frac{\left[\theta\left(\theta^2q^2+2\theta q+2\right)+\left(\theta^3q^3+3\theta^2q^2+6\theta q+6\right)\right]e^{-\theta q}}{2(\theta+3)}\right] \tag{19}$$

and

$$L(p) = 1 - \frac{\left[\theta\left(\theta^2q^2+2\theta q+2\right)+\left(\theta^3q^3+3\theta^2q^2+6\theta q+6\right)\right]e^{-\theta q}}{2(\theta+3)} \tag{20}$$

2.4 *Order Statistics*

Let $x_1, x_2, \ldots x_n$ be a random sample of size n from the proposed distribution. Let $X_{(1)} < X_{(2)} < \cdots < X_{(n)}$ denote the corresponding order statistics. The p.d.f. and the c.d.f. of the k th order statistic, say $Y = X_{(k)}$ are given by

$$f_Y(y) = \frac{n!}{(k-1)!(n-k)!}F^{k-1}(y)\{1-F(y)\}^{n-k}f(y)$$

or

$$f_Y(y) = \frac{n!}{(k-1)!(n-k)!}\sum_{l=0}^{n-k}\binom{n-k}{l}(-1)^l F^{k+l-1}(y)f(y) \tag{21}$$

and

$$F_Y(y) = \sum_{j=k}^{n}\binom{n}{j}F^j(y)\{1-F(y)\}^{n-j}$$

or

$$F_Y(y) = \sum_{i=k}^{n}\sum_{l=0}^{n-j}\binom{n}{j}\binom{n-i}{l}(-1)^l F^{i+l}(y) \tag{22}$$

Now, using equation number (1) and (2) in equation (21) and (22), we get the corresponding pdf and the cdf of $k-th$ order statistics of the proposed distribution that can be written as

$$f_Y(y) = \frac{n!}{(k-1)!(n-k)!}\sum_{l=0}^{n-k}\sum_{m=0}^{k+l-1}\binom{n-k}{l}\binom{k+l-1}{m}(-1)^{l+m}$$
$$\left(\frac{\theta^3}{\theta+2}\right)\left[\frac{\left[\theta(1+\theta y)+(\theta^2y^2+2\theta y+2)\right]e^{-\theta y}}{\theta+2}\right]^m (y+y^2)e^{-\theta y} \tag{23}$$

and

$$F_Y(y) = \sum_{i=k}^{n}\sum_{l=0}^{n-i}\sum_{m=0}^{i+l}\binom{n}{i}\binom{n-i}{l}\binom{i+l}{m}(-1)^{l+m}$$
$$\left[\frac{\left[\theta(1+\theta y)+(\theta^2y^2+2\theta y+2)\right]e^{-\theta y}}{\theta+2}\right]^m \tag{24}$$

3 Estimation of the parameter

Above discussed distribution is of one parameter which is estimated by method of maximum likelihood. The likelihood function for the proposed distribution can be written as

$$L(\theta) = \prod_{i=1}^{n}\left[\frac{\theta^3}{\theta+2}\right]e^{-\theta x_i}(x_i+x_i^2)$$

or

$$L(\theta) = \left[\frac{\theta^{3n}}{(\theta+2)^n}\right]e^{-\theta\sum_{i=1}^{n}x_i}\prod_{i=1}^{n}(x_i+x_i^2)$$

Now, log-likelihood can be given as

$$\log L(\theta) = 3n\log\theta - n\log(\theta+2) - \theta\sum_{i=1}^{n}x_i + \sum_{i=1}^{n}\log(x_i+x_i^2)$$

Differentiating the above equation with respect to θ partially, we get,

$$\frac{\partial \log L}{\partial\theta} = \frac{3n}{\theta} - \frac{n}{\theta+2} - \sum_{i=1}^{n}x_i \tag{25}$$

Equating zero and solving equation (25) for θ, we get the mle of θ,

$$\hat{\theta} = \frac{\sqrt{\bar{x}^2+4\bar{x}+1}-(\bar{x}-1)}{\bar{x}} \tag{26}$$

4 Total time on test (TTT)

We know that distribution function $F(t)$ and and μ the mean time to failure (MTTF). The $F(t)$ is continuous and strictly increasing which indicates that $F^{-1}(t)$ exists. thus the Total time on test (TTT) of $F(t)$ is defined as

$$\phi(x) = \frac{1}{\mu}\int_0^{F^{-1}(x)}[1-F(t)]\,dt \quad \text{for} \quad 0 \le \mu \le 1 \tag{27}$$

The value of $\phi(x)$ is interpreted as the area below $\frac{1-F(t)}{\mu}$ between 0 and $F^{-1}(\mu)$. The TTT plot, an empirical and scale independent plot based on failure data and corresponding to asymptotic curve, The scaled TTT-transformation see [17] is used to illustrate some test statistics for testing exponentiality.

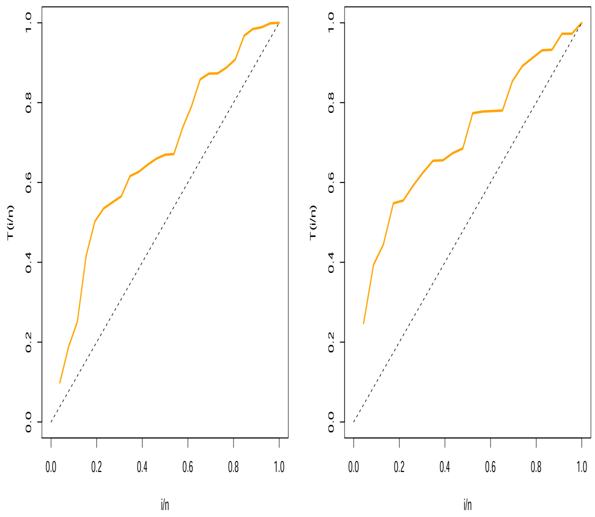

Fig. 5: TTT-plot for 1st and 2nd dataset of mLAE

The TTT plot shown in the figure 5 for first and second data sets is both convex which gives an indication of monotonically increasing failure rate function to fit mLAE distribution.

5 Application on Real Data

The applications of the proposed distribution have been discussed with the two data sets, one from medical science and another from engineering science. First data set is taken from the ovarian cancer patients, this dataset consists of survival time (in days) of 26 ovarian cancer patient having all tumour masses greater than 2cm (in diameter) after their surgical treatment of ovarian cancer and this dataset is propose by [18]. The second data set is from [19]. The data given arose in tests on endurance of deep groove ball bearings. The data are the number of million revolutions before failure for each of the 23 ball bearings in the life tests. Summary measure of both the data sets are shown in Table (1). It is reveals that both the data sets are under dispersed and positively skewed. For the above two dataset, proposed distribution has been fitted along with two-parameter distributions Quasi lindley distribution by [20], a two parameter lifetime distribution with buthtub hazard rate named as Chen distribution, see [21], and one parameter lifetime distributions including exponential, Lindley, logarithmic transformed exponential (LTE) distribution [22], exponentiatial transfomed Lindley (ETL) [23], DUS transformation of Exp(θ)- distribution by [24], length biased exponential distribution (LBED) used in [25]. The ML estimates along with $-2\log L$, Akaike Information criteria (AIC), Corrected Akaike Information criteria (AICc) see [26], K-S statistics and p-value of the fitted distributions are presented in table number (2) and (3). The AIC, BIC, AICc and K-S Statistics are computed using the following formulae:

$$AIC = -2loglik + 2k, \qquad BIC = -2loglik + k\log n$$

$$AICc = AIC + \frac{2k^2 + 2k}{n-k-1}, \qquad D = \sup_x |F_n(x) - F_0(x)|$$

where k= the number of parameters, n= the sample size, and the $F_n(x)$=empirical distribution function and $F_0(x) =$ is the theoretical cumulativedistribution function. The best distribution is the distribution corresponding to lower values of$-2\log L$, AIC, BIC, AICc and K-S statistics and higher p-value.

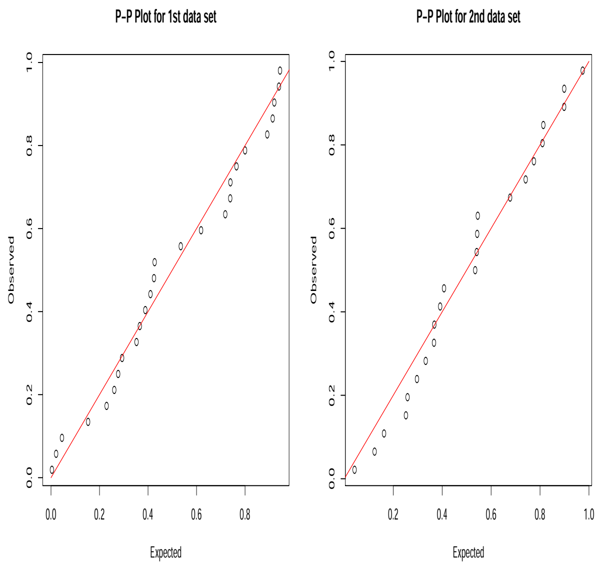

Fig. 6: pp-plot for 1st and 2nd dataset of mLAE

The formal goodness of fit test is applied and display in Table no (2) and (3) in order to verify better performance of distribution to the data. Also pp-plot for the data sets are displayed in the Figure 6.

6 Conclusion

In this paper some popular and widely used distributions have been discussed along with the proposed mLAE distribution. Since the datasets are increasing hazard type, we considered nine distributions with increasing hazard and we notice that one parameter mLAE distribution is better in comparison to other distributions on the basis of various model selection criterion, K-S statistics and

Table 1: Summary of the two datasets.

Dataset	n	mean	s.d	median	skewness	kurtosis	min	max
Overian cancer data	26	599.53	339.69	476.00	0.4136	2.1537	59.000	1227.0
Ball bearings data	23	72.229	37.480	3.4888	0.9419	3.4888	17.880	173.40

Table 2: MLE's, - 2ln L, AIC, K-S and p-values of the fitted distributions for the ovarian cancer dataset.

Distribution	Estimate		-2LL	AIC	BIC	AICc	K-S	p-value
	α	θ						
mLAE		0.0049	374.57	376.57	377.83	376.73	0.1115	0.8675
DUSE		0.0022	380.53	382.53	383.79	382.70	0.2334	0.0995
QLD	-0.1184	0.0036	374.60	378.60	381.11	379.12	0.1243	0.7717
Chen	0.0012	0.2915	373.09	377.09	379.61	377.62	0.1550	0.5106
LBED		0.0033	375.18	377.18	378.43	377.34	0.1461	0.5847
ETL		0.0039	373.92	375.92	377.18	376.09	0.1138	0.8520
LTE		0.0020	382.08	384.08	385.34	384.25	0.2519	0.0610
Lindley		0.0033	375.20	377.20	378.46	377.37	0.1467	0.5800
Exponential		0.0017	384.60	386.60	387.86	386.77	0.2684	0.0382

Table 3: MLE's, - 2ln L, AIC, K-S and p-values of the fitted distributions for the ball bearings dataset.

Distribution	Estimate		-2LL	AIC	BIC	AICc	K-S	p-value
	α	θ						
mLAE		0.0412	227.15	229.16	230.29	229.34	0.1211	0.8491
DUSE		0.0182	238.47	240.47	241.61	240.66	0.2774	0.0467
QLD	3.0478	0.0177	241.80	245.80	248.07	246.40	0.1822	0.3036
Chen	0.0044	0.3803	230.57	234.57	236.84	235.17	0.1711	0.4608
LBED		0.0277	231.05	233.05	234.18	233.24	0.1887	0.3422
ETL		0.0332	229.60	231.60	232.73	231.78	0.1662	0.4975
LTE		0.0172	240.27	242.27	243.41	242.46	0.2943	0.0292
Lindley		0.0273	231.47	233.47	234.61	233.66	0.1928	0.3175
Exponential		0.0138	242.87	244.87	246.01	245.06	0.3068	0.0203

associated p-value. Although the ETL distribution perform well for ovarian cancer data but it is complicated than the proposed mLAE distribution. For the second data i.e. from engineering science, the proposed mLAE distribution undoubtedly best among all other distributions in the present study. It can also be used further to develop various new probability models according to the real life situations.

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Conflict of interest

There is no conflict of interest.

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