ESTIMATION OF A INCUBATION PERIOD BETWEEN HIV TO AIDS –A STUDY OF VIJAYAPUR DISTRICT

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ESTIMATION OF A INCUBATION PERIOD BETWEEN HIV TO AIDS -A STUDY OF VIJAYAPUR DISTRICT

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ABSTRACT:

INTRODUCTION: One of the worst ways for the population to be worried is to die from disease. In that several thousands of deaths occurred because of dreadful infectious diseases. The challenges faced by the present day world is pandemic of acquired Immune deficiency syndrome.

The Acquired Immune Deficiency syndrome (AIDS) is a distressing disease affected by Human Immune deficiency virus (HIV), spread through sexual contacts or other interactions in which body fluids are exchanged or using contaminated blood products. **Need of the study:** The use of statistical modeling approaches make a valuable contribution for developing better understanding of the levels and trends in the HIV epidemic and the limited information based on the estimates. **AIMS &OBJECTIVES:** To estimate the incubation time distribution of HIV to onset of AIDS.**Methodology**:Retrospectiveand prospective study was doneonpatientsunderthefollow-upofARTatCivil hospital between 2016and 2020, Vijaypur, Karnataka **Result:** The average incubation period for all patients in the current investigation was 2080.3 (with a median of 2210) days, with a 95 percent confidence interval of (2006.6 – 2154.0). **Conclusions:** The best fitted probability distribution for incubation period from HIV to AIDS for overall participants was Cauchy distribution model.

Keywords: Cauchy distribution, HIV/AIDS,,Incubation Period, Models fitting, Weibulldistribution.

Introduction

AIDS (acquired Immune deficiency syndrome) caused by Human immunodeficiency virus has become one of the world's greatest challenge ever since the first cases was reported in 1981. Over 75 million people have been infected with HIV(1) and millions of people have died due to AIDS-related causes since the beginning of the epidemic.(2) According to the UNAID Global HIV & AIDS statistics — 2020 fact sheet it was estimated that there are over 38.0 million [31.6 million–44.5 million] people globally, were living with HIV in 2019 and 690 000 people have died from AIDS-related illnesses in 2019. In India HIV infection was first detected in 1986 [1] . Ever since then India has become home to third largest population of people living with HIV and AIDS. According to the estimation done by UNAID 2017 there are over 2.1 million people, currently living with HIV in India and over 69 000 people died from an AIDS-related illness. (2) According to the HIV estimation report by NACO 2017, Karnataka is ranked fifth with HIV prevalence of 0.47%, and 2.47 Lakh people living with HIV. (3)In Vijaypur district, around 1,79,272 people were tested for HIV, of them 19,044 were found to be positive. Registered 1,620 cases of death due to AIDS in 2013. (1)

Need of the study**:**For Public health HIV/AIDS become one of the most important challenges. It was first recognized in United States almost two decades back. To resolve large scale health issues of the world, statistical methods have expanded spatially. These methods have a major role in the study of the HIV/AIDS pandemic. It is well known that HIV/AIDS is an incurable epidemic and a successful treatment has not been revealed as yet. Hence to stop the spread of this deadly epidemic active precautionary measures have to be taken with thorough care. In order to determine the current levels and trends in this epidemic, access to the related and comprehensive research data is pertinent. Due to the stigma of this disease, gathering precise information on prevalence and incidence is difficult. The use of statistical modeling approaches make a valuable contribution for developing better understanding of the levels and trends in the HIV epidemic and the limited information based on the estimates. The aim of any modeling is to dig out as much as information feasible from existing data. The application of statistical modelling methodologies contributes significantly to a better understanding of the HIV epidemic's levels and trends, as well as the limited information available based on estimations.

Meterial and Methods:

Thestudywasretrospective and prospective doneonpatientsunderthefollowupofARTatCivil hospital between 2016and 2020, Vijaypur, Karnataka.

The requisitedata wascollectedfromtheART centre, Civil Hospital, Vijaypur district on HIV/AIDS. Total screened cases (Registered) during study period were 1796. Among them 641 cases were developed AIDS during study period. Thepatientswhowere transferredtootherhealthinstitutionaftertheinitiationoffree ART and patientswhosediagnosisyearormonth was missingand those patientswhose deathmonthwasmissingwereexcludedfrom thestudy. Forfindingtheincubationtimedistribution, thedataof641 HIV/AIDSpatientswereretrievedfromtheHospitalrecord.

All variables considered in this study have been extracted from the hospital records. The variables collected were age, gender, occupation, mode of spread, date of AIDS diagnosed, and date of death. The data were collected by the principal investigator and trained nurses.

Statistical analysis: Descriptive statistics such as mean, SD and percentage was used to present the data. The incubation period is defined as the time between the infections to onset of the disease. HIV incubation period is the random time between the HIV infection and the onset of clinical AIDS symptoms. Here we calculated incubation period in days by taking difference of HIV infection and the onset of clinical AIDS symptoms. The calculation of 95% CI for Kaplan-Meier probabilities was based on their standard error estimates computed with Greenwood's formula.

Thedatawas analysed usingExcel2007,Easy Fit 5.6 Professional,and StatisticalPackageforthe Social Sciences(SPSS)forWindowsVersion16.0(SPSSInc;Chicago,IL,USA)and EPIInfo3.5.1windowsversion.Ap-valueof< 0.01(two-tailed)fordistribution fittingand<0.05(two-tailed)forrestallwereusedto establishstatistical significance.

Commonlyusedmodelsfor theincubationperiodof HIV/AIDS:

TheyareWeibullmodel, Gammamodel, Log normal model, Logisticmodel etc. Present studyexplainsthecharacterizationproperties, asymmetry, skewness and kurtosis ofthe bestfittedmodelthedatafromtheseveralstatisticaldistributions.

Results:

Out of 1796 screened population of HIV/AIDS during study period, there were 933(51.9%) participants of stage I, 140 (7.8%) participants of stage II and 723(40.3%) cases of stage III. Attendance of ART center was more common in Male (53.7%) than female (46.3%). (Table 1). There were 179(10%) participants in the age group 1 to 12 years, 1529(85.1%) participants in the age group 13 to 49 years, 87(4.8%) participants in the age group 50 to 69 years and only one case in the age group above 69 years. Maximum number of participants were observed in 13 to 49 years age group and least in the age group above 69 years, (Table 2). Among various modes of spread of HIV in all stages, most common modes of transmission was found Heterosexuality (86.6%) followed by vertical transfusion (10.2%). There was least transmission by Blood transfusion (0.1%) (TABLE 3).Incidence of AIDS was found more in male (58%) than female (42%) this difference was statistically significant ($p<0.01$). There was an increasing trend observed in occurrence of HIV cases during study period.

Amongtotal screened population,641participants werehaddevelopedAIDS duringfollowup,ofwhom117haddied.Overall,the meanageofthe385 males(31.7 years)was similartothatinthe256females(28.19years).

For overall patients who developed HIV and then AIDS occurred during the study period, the average incubation period was found to be 2080.3 days with 95% C.I. (2006.6 – 2154.0) days. (Table 4). The best statistical distribution that fits for incubation period was assessed by applying goodness of fit test by using Kolmogorov Smirnov, Anderson Darling and Chi-squared methods, and it was found that, the best fitted probability distribution for incubation period from HIV to AIDS for overall participants was Cauchy distribution model (Table-5& 6). For present study, parametric values of incubation period distributions from HIV to AIDS in overall participants for Cauchy distribution model is $\mu=339.63$ σ(sigma) =2250.1.

The average incubation period of HIV adults who diagnosed as AIDS was found to be 2401.2 days with 95% C.I. (2353.1 days to 2449.3 days). The best statistical distribution that fits the incubation period was assessed by applying goodness of fit test Parametric values of incubation period from HIV to AIDS for Adults and Pediatrics were estimated by various statistical probability distributions. The best fitted probability distribution for incubation period from HIV to AIDS for Adults was Burr distribution model.

For pediatric age group, who developed HIV and then diagnosed as AIDS the average incubation period was found to be 180.01 days with 95% C.I. (123.44 – 236.58) days. The best statistical distribution that fits the incubation period was assessed by applying goodness of fit test. The best fitted probability distribution for incubation period from HIV to AIDS for pediatric patients was Lognormal (3P) distribution model.

Discussion:

Distribution of incubation period is very difficult to estimate, as infection time is usually unknown. Moreover in India the exact time of HIV is difficult to know because of awareness about the disease and lack of medical facilities. To estimate HIV incidence, mathematical and statistical models can be used. On the basis of authentic HIV prevalence and on some assumptions regarding survival after onset of disease, several models have been developed over a time. Some of the models developed are Techniques such as back calculation, dynamic and demographic models, and birth cohort approaches[4-6]to estimate HIV incidence epidemic, the most common methods suggested by UNAIDS/WHO are Estimation and Projection Package (EPP) and Spectrum AIDS Impact Model. These methods have been used in more than 120 countries worldwide toprovide national, regional andglobal estimates ofthe impactofHIV.

In Vijayapur District there are large discrepancies between observed and estimated number of HIV and AIDs cases. Our research is the first of its kind in terms of determining the best-fit statistical distribution for HIV incubation time.

The maximum number of HIV cases was observed in 13 – 49 years of age group and least in the age group of 70 and above. Incidence of HIV was significantly more ($p<0.01$) in Male than Female. There was an increasing trend observed in occurrence of HIV cases during the study period. Most common modes of transmission of HIV/AIDS were heterosexuality followed by vertical transfusion .The most affected age group for HIV/AIDS was younger age group. Mostly in between 25-45.

For overall patients who developed HIV and then AIDS occurred during the study period, the average incubation period was found to be 2080.3 (median 2210) days, with 95% C.I. (2006.6 – 2154.0). This is very less as compared to other study conducted by Peter Bacchetti and Moss AR, (7) the median incubation period was 9.8 years. Medley et al; (8) showed that the incubation period from infection of disease to diagnosis of AIDS is lengthy and changeable, depends on patient age & sex; approximately 8 years.

Bachetti (1990) (9) and Bachetti and Jewell (1991) (10) provide non parametric estimated of AIDS incubation distribution using data from San Francisco Cohorts, estimated median time to AIDS between 10 & 11 years.

However, age has been found to be significantly associated with an incubation period. Many studies showed that the less rapid progression of disease in younger than those who were older at the time of infection (The Italian seroconversion groupSelwyn et al, 1992(11), Mientjes et al 1993(12)). Andrea P et al, 1992 (13), Manotto et al, 1992(14), In the current study the average incubation period of HIV adults who diagnosed as AIDS was found to be 2401.2 days (5.7 Years) with 95% C.I. (2353.1 days to 2449.3 days). The best statistical distribution that fits the incubation period was assessed by applying goodness of fit test Parametric values of incubation period from HIV to AIDS for Adults were estimated by various statistical probability distributions. A Burr distribution model was the best fit probability distribution for the incubation period from HIV to AIDS in Adults.

Conclusion:

The best statistical distribution that fits the incubation period was assessed by applying goodness of fit test, the best fitted probability distribution for incubation period from HIV to AIDS for overall participants was Cauchy distribution model. The best fitted probability distribution for incubation period from AIDS to Deaths for overall age group was Log-Pearson 3 model. The best fitted probability distribution for incubation period from HIV to AIDS for paediatric patients was Lognormal (3P) distribution model. The best fitted probability distribution for incubation period from HIV to AIDS for Adults was Burr distribution model.

Recommendation:

During this epidemic, bestfeasibleinformationisextremely necessary todeterminethecurrent levels andtrends. The application of statistical modelling methodologies makes a valuable contribution to developing a better knowledge of the levels and trends in the HIV epidemic, as well as the limited information based on estimations. Estimates of thetotal number of prevalentHIV infections attributable tothe majorrouteof infectionmakean importantcontributiontopublichealthpolicy. Theycanbeusedfor the planningofhealth careservices.

Limitations of the study:

Thisstudyhadsomelimitations:thefirstisthatthestudy useddatafromonlyone hospital. Thus, thefindings ofthis studyshould beinterpreted verycarefullywhenplan to use and inferatnational level. The second and severe limitation of the study is a limited availability of information on HIV/AIDS. The nature of available data, to a great extent, tailored the direction of this study. The data were collected on all HIV tested positive cases between November 2016 and December 2020.

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Table - 1: Basic characteristics of the patients

Basic variables	**No. of patients**	**Percentage**
Gender		
Male	965	53.7
Female	831	46.3
Age(Years)		
1 - 12	179	10.0
13 - 49	1529	85.1
50- 69	87	4.8
≥ 70	1	0.1
Mode of spread		
Hetero sexual	1555	87.6
Vertical transfusion	183	10.2
Men with men	24	1.3
Sex worker	24	1.3
Injecting drug	5	0.28

Blood transfusion	1	0.05
Unknown	4	0.22
Total	1796	100.0

Table – 2: Descriptive statistics showing incubation period from HIV to AIDS in overall participants

Statistic	Value	Percentile	Value
Sample Size	641	Min	3
Range	6437	5%	32.4
Mean	**2080.3**	10%	174.4
Variance	9.0642E+5	25% (Q1)	1867.5
Std. Deviation	952.06	50% (Median)	**2210**
Coefficient. of Variation	0.45766	75% (Q3)	2557.5
Std. Error	37.604	90%	2970.6
Skewness	-0.55743	95%	3407.6
Excess Kurtosis	1.2826	Max	6440

Table – 3: Goodness of fit –summary by Kolmogorov Smirnov, Anderson Darling and Chi-squared method of various probability distributions fitted to incubation period from HIV to AIDS in overall participants

#	Distribution	Kolmogorov Smirnov		Anderson Darling		Chi-Squared	
		Statistic	Rank	Statistic	Rank	Statistic	Rank
1	Beta	0.16643	17	29.232	13	241.4	13
2	Burr	0.28484	35	81.739	26	564.9	30
3	Burr (4P)	0.16227	15	26.644	12	227.2	11
4	**Cauchy**	**0.07363**	**1**	**6.1776**	**1**	**15.907**	**1**
5	Chi-Squared	0.48251	51	2484.5	57	1910.8	45
6	Chi-Squared (2P)	0.51003	53	4445.3	58	2027.8	46
7	Dagum	0.2942	36	69.041	22	412.23	24
8	Dagum (4P)	0.5352	54	264.95	46	N/A	
9	Erlang	0.37764	43	196.75	44	567.37	31
10	Erlang (3P)	0.19522	21	37.598	18	265.23	18
11	Error	0.15019	8	23.144	7	171.18	6
12	Error Function	0.79099	58	1572.0	56	8399.7	52
13	Exponential	0.37797	45	106.63	32	1158.9	38

14	Exponential (2P)	0.37784	44	111.21	34	1164.2	39
15	Fatigue Life	0.57842	55	279.59	47	2999.9	50
16	Fatigue Life (3P)	1	60	N/A		N/A	
17	Frechet	0.43106	50	145.16	43	2920.7	49
18	Frechet (3P)	0.23511	28	54.818	20	507.33	28
19	Gamma	0.22846	25	130.78	40	334.63	22
20	Gamma (3P)	0.18744	20	35.557	17	271.88	20
21	Gen. Extreme Value	0.12177	4	111.37	35	N/A	
22	Gen. Gamma	0.35845	41	108.26	33	994.33	36
23	Gen. Gamma (4P)	0.1461	7	25.615	10	225.43	10
24	Gen. Pareto	0.15745	11	296.72	51	N/A	
25	Gumbel Max	0.23406	27	89.129	27	332.08	21
26	Gumbel Min	0.1078	2	19.809	3	163.31	4
27	Hypersecant	0.15262	9	22.857	6	165.87	5
28	Inv. Gaussian	0.25204	30	610.62	55	372.56	23
29	Inv. Gaussian (3P)	0.21673	24	597.35	54	N/A	
30	Johnson SU	0.13441	6	19.123	2	178.3	7

31	Kumaraswamy	0.15888	12	25.604	9	247.48	14
32	Laplace	0.12989	5	20.489	4	120.92	2
33	Levy	0.59056	56	284.33	49	1078.4	37
34	Levy (2P)	0.38921	47	128.55	39	2480.4	48
35	Log-Gamma	0.4032	48	139.62	42	1887.7	44
36	Log-Logistic	0.37196	42	114.82	37	2136.4	47
37	Log-Logistic (3P)	0.10839	3	21.352	5	143.64	3
38	Log-Pearson 3	0.27927	33	113.52	36	N/A	
39	Logistic	0.16012	14	25.292	8	196.35	8
40	Lognormal	0.37829	46	119.24	38	1853.3	43
41	Lognormal (3P)	0.17584	19	32.493	16	256.38	16
42	Nakagami	0.15391	10	104.67	31	202.23	9
43	Normal	0.17054	18	30.198	14	248.42	15
44	Pareto	0.486	52	212.95	45	630.25	33
45	Pareto 2	0.42474	49	133.38	41	1248.8	40

46	Pearson 5	0.30759	38	280.21	48	424.8	26
47	Pearson 5 (3P)	0.33479	39	290.66	50	581.76	32
48	Pearson 6	0.34295	40	97.556	29	951.21	35
49	Pearson 6 (4P)	0.15897	13	31.539	15	264.63	17
50	Pert	0.24337	29	53.288	19	548.34	29
51	Power Function	0.28132	34	91.031	28	1351.3	41
52	Rayleigh	0.23226	26	73.293	24	421.59	25
53	Rayleigh (2P)	0.27502	31	61.224	21	484.38	27
54	Reciprocal	0.65822	57	448.89	53	3120.3	51
55	Rice	0.20502	22	69.313	23	269.69	19
56	Student's t	0.98614	59	8384.1	59	1.2868 E+5	53
57	Triangular	0.27668	32	75.582	25	854.71	34
58	Uniform	0.20506	23	334.64	52	N/A	
59	Weibull	0.30503	37	99.069	30	1585.7	42
60	Weibull (3P)	0.16228	16	25.757	11	239.0	12
61	Johnson SB	No fit					

Table 4:Goodness of Fit-Details

Cauchy					
Kolmogorov-Smirnov					
Sample Size	641				
Statistic	0.07363				
P-Value	0.00181				
Rank	1				
α	0.2	0.1	0.05		
Critical Value	0.04238	0.04831	0.05364		
Reject?	Yes	Yes	Yes		
Anderson-Darling					
Sample Size	641				
Statistic	6.1776				
Rank	1				
α	0.2	0.1	0.05	0.02	0.01
Critical Value	1.3749	1.9286	2.5018	3.2892	3.9074
Reject?	Yes	Yes	Yes	Yes	Yes
Chi-Squared					
Deg. of freedom	9				
Statistic	15.907				
P-Value	0.06886				

Rank	1				
α	0.2	0.1	0.05	0.02	0.01
Critical Value	12.242	14.684	16.919	19.679	21.666
Reject?	Yes	Yes	No	No	No

Figure 1: Probability density function of Cauchy distribution model

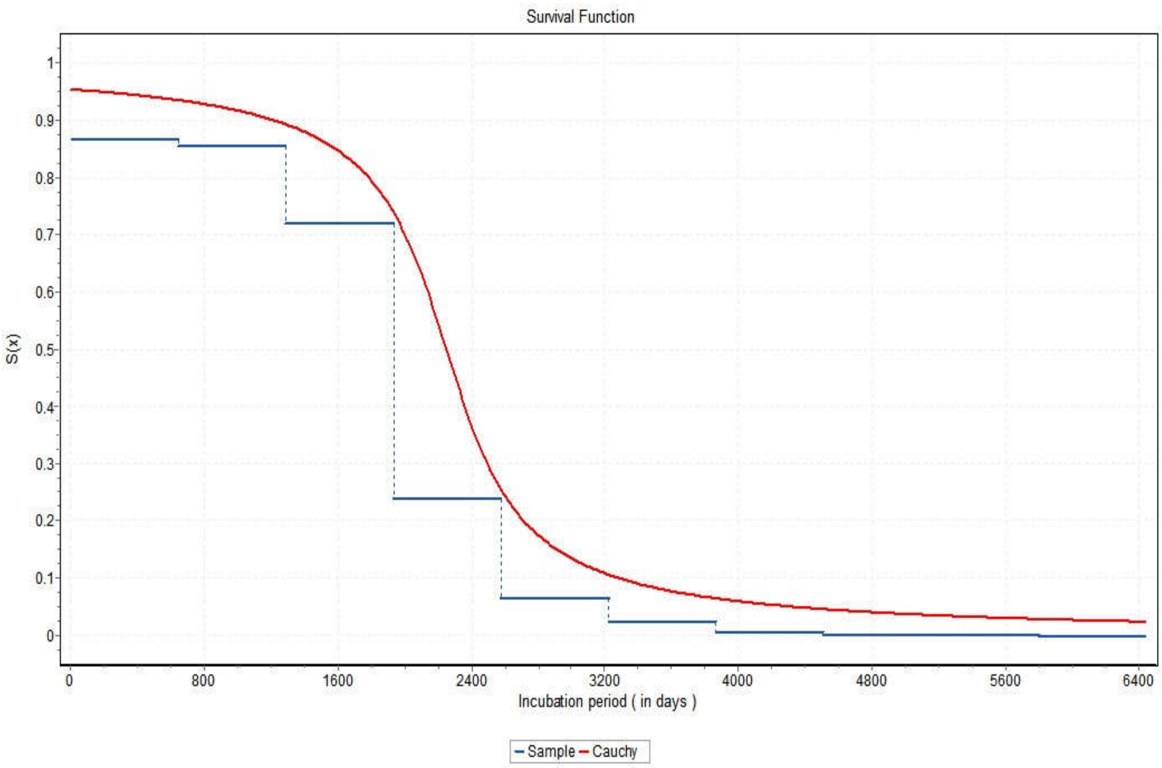
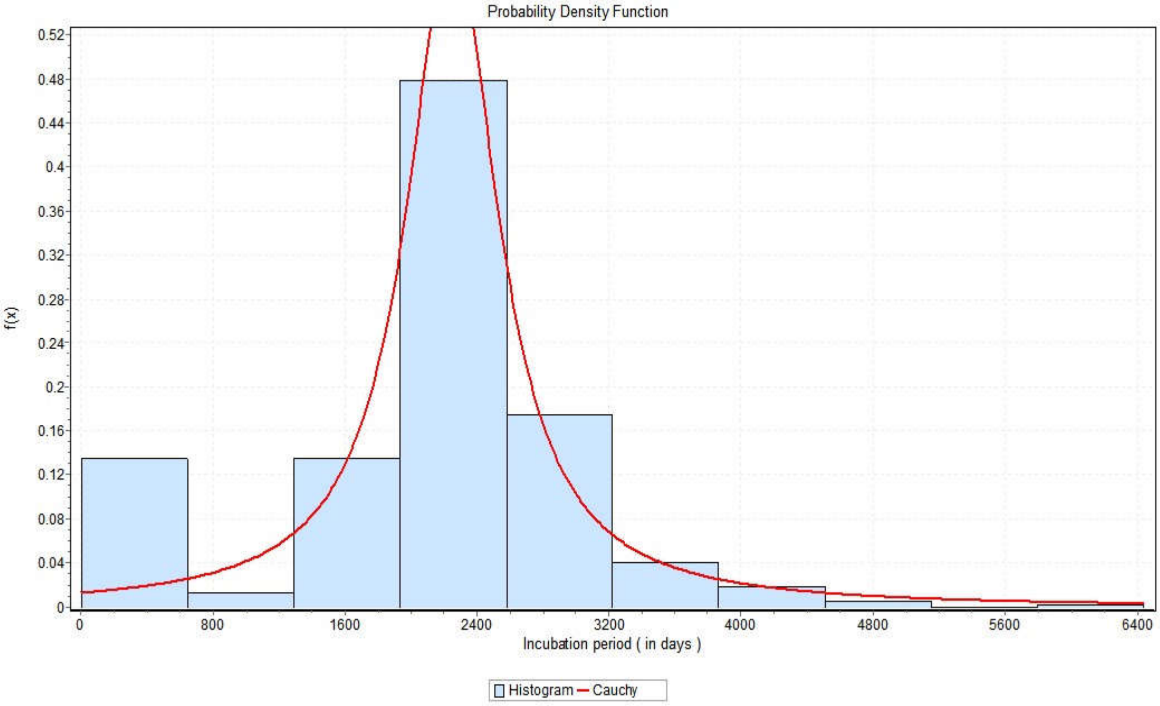


Figure 2: Survival function of Cauchy distribution model


Probability Density Function
f(x)
0.52
0.48
0.44
0.4
0.36
0.32
0.28
0.24
0.2
0.16
0.12
0.08
0.04
0
0
800
1600
2400
3200
4000
4800
5600
6400
Incubation period (in days)
Histogram
Cauchy