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# Application of Statistical Methods in Pharmacology

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**ABSTRACT:** In this paper we estimate the number of patients to have a particular type of remedy like no relief, one percent to fifty percent relief, fifty one percent to ninety percent relief and ninety one to hundred percent relief after administering the drug manufactured by a firm for curing a disease so that its curing capacity is on par with drugs produced by other two firms which are known to be best medicine for curing the same disease. These estimations are obtained using the Chi-square goodness of fit and they were shown graphically for various fixed number of patients with no relief and total relief. It helps the firm to decide whether modification of drug is required or not. Further a matlab program is written to give the output "on par with the two medicines" or "not on par with these two medicines" taking the input data of number of patients of each type.

**INTRODUCTION:**

Statistical methods have been applied in various fields such as pharmaceutical industry, medicine, quality control, biological sciences and economics. Testing of hypothesis is one of the tools in statistical methods. It is can be used in pharmacological research to determine whether the pharmacological effect of one drug is superior to another or equivalent. The use of Statistics in pharmacology was discussed by D.Spina[1] and some examples of the use of statistics in Pharmacology are given by C.V. Winder [2]. The graph (Fig.10) of [3] showing the probabilities of there being n=0are computed for various times is similar to the graph (Fig.2.2) of [4] which is drawn concentration and dosage response curves. The different companies manufacture variety of drugs to cure a disease. If a drug manufactured by a company is not good with respect to curing the disease then the company has to make certain modifications in the medicine to improve the curing capacity of the disease. Researchers in the quality control of pharmaceutical industry have to modify the drug effect by combining it with another drug or add some other substance to the existing composition to improve its curing capacity of the disease. Pharmacoepidemiology is the study of effects of drugs and it is useful to improve the curing capacity of the drug. The medicine with new composition has to be tested with the patients. The present paper helps the researchers to verify the curing capacity of the medicine with other two medicines which are supposed to good in curing the disease. The amount of relief to the patients is different from a patient to another because of their resistance power and other conditions or not following the instructions given by doctor. Therefore, we divided the amount of relief as no relief, 1% to 50%, 51% to 90% and 91% to 100% relief. We refer these types of reliefs as type-1, type-2, type-3 and type-4 respectively.

In this paper, we considered the data of two medicines Y and Z produced by two companies in curing the disease and they are supposed to be good in curing the disease. Chi-square goodness of fit given in text Kapoor [5] is used to test whether they have equal effect on curing the disease. The bounds for the number of patients with no relief by the new or modified medicine X are estimated using the Chi-square goodness of fit. Such tests are useful for the researchers who are preparing or modifying the drug to make it on par with medicines Y and Z. We have considered the data of two medicines Y and Z for curing the disease after administering these medicines to hundred patients each. The data contains the number of patients having remedy of type-1, type-2, type-3 and type-4. We take the number of patients with no relief as one parameter and the number of patients with total relief as another parameter. Assigning some particular values to these parameters, we have obtained the possible values of number of patients with other two types of relief so that the new medicine or modified drug will have same effect as that of two medicines Y and Z in curing the disease.

It is observed that if the number of patients of type-1 is 3 and number of patients of type-4 is 20 , we have obtained the possible values of number of patients of type-2 and type-3 are (10, 67),(11, 66),……(31,46) so that the medicine X will have the same curing capacity of the medicines Y and Z. The data collected on experimenting the medicine can be compared with theoretical results and can make a conclusion about its curing capacity as that of other two medicines which are supposed to be good. A matlab program is written to give the output “On par with two medicines” or “Not on par with two medicines” by taking the complete data of number of patients of each type.

**MATERIALS:**

The following is the data pertaining to the number of patients of type-1, type-2, type-3 and type-4 relief of 100 patients each after the consumption of the Drug Y and Drug Z which are produced by the companies B and C.

| % of curing the disease | Drug Y | Drug Z | Total |
|---|---|---|---|
| | Observed | Observed | |
| No relief | 2 | 7 | 9 |
| 1 % to 50% | 16 | 18 | 34 |

| | | | |
|---|---|---|---|
| 51% to 90% | 53 | 46 | 99 |
| 91 % to 100 % | 29 | 29 | 58 |
| Total | 100 | 100 | 200 |

**Methods:**

We set up the null hypothesis $H_0$ : The drugs Y and Z have equal effective in curing the disease. The computed expected frequencies are shown in the following table.

| | Drug Y | | Drug Z | | Total |
|---|---|---|---|---|---|
| | Observed | Expected | Observed | Expected | Observed |
| No relief | 2 | 4 | 7 | 5 | 9 |
| 1 % to 50% | 16 | 17 | 18 | 17 | 34 |
| 51% to 90% | 53 | 50 | 46 | 50 | 99 |
| 91 % to 100 % | 29 | 29 | 29 | 28 | 58 |
| Total | 100 | 100 | 100 | 100 | 200 |

The Chi-square is defined as $\chi^2 = \sum (O_i - E_i)^2 / E_i$ and the calculated Chi-square value is 2.4534. From the Chi-square tables $\chi^2$ tabulated value is 7.815 at 5% level of significance with 3 degrees of freedom. Since $\chi_{cal}^2 < \chi_{tab}^2$, the null hypothesis can't be rejected. Therefore, we conclude that the drugs Y and Z produced by the companies B and C are equally effective in curing the disease.

Suppose if a company A wishes to produce or modify the drug X so that the drug X will have equal capacity of curing the disease as to that of drugs Y and Z then drug manufactured by the company A has to administer the drug to 100 patients and collect the number of patients p ,q, r and s where p is the number of patients of type-1 remedy, q be the number of patients with type-2 remedy, r be the number of patients with type-3 remedy and s be the number of patients with type-4 remedy.

**Case (i): Number of patients of p= 3 and s=20**

Suppose the numbers of patients with type-1 and type-4 cure are 3 and 20. We wish to know the possible values of q and r so that the medicine X shall have the same curing capacity as that of medicine Y and Z. Table-1 shows the number of patients of type-2 and type-3 Chi square value three attributes. If the values of q and r in a row against the chi square value that is less than tabulated chi square value 12.592 then we can consider the drug is on par with

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the other two medicines. From the statistical tables the $\chi^2$ value for 6 degrees of freedom is 12.592 at five percent level of significance.

For example p=3,q=10, r=67,s=20 medicine X will have same curing capacity as that of medicines Y and Z since $\chi^2$ calculated is less than $\chi^2$ tabulated value . Similarly p=3,q=11, r=66,s=20,….,and p=3,q=24, r=53,s=20(see Fig.1).

**Table-1: Table showing q, r and Chi-square values for fixed p=3 and s=20**

| Number of patients | | Chi square value | Number of patients | | Chi square value |
|---|---|---|---|---|---|
| q | r | | q | r | |
| 1 | 76 | 28.49359 | 40 | 37 | 22.64359 |
| 2 | 75 | 26.14014 | 41 | 36 | 24.26137 |
| 3 | 74 | 23.98784 | 42 | 35 | 26.00359 |
| 4 | 73 | 21.31781 | 43 | 34 | 27.20455 |
| 5 | 72 | 19.46626 | 44 | 33 | 29.02797 |
| 6 | 71 | 17.80364 | 45 | 32 | 30.97378 |
| 7 | 70 | 15.95192 | 46 | 31 | 32.3125 |
| 8 | 69 | 14.54121 | 47 | 30 | 34.33834 |
| 9 | 68 | 13.30907 | 48 | 29 | 36.48476 |
| 10 | 67 | 12.07389 | 49 | 28 | 37.96978 |
| 11 | 66 | 11.05571 | 50 | 27 | 40.19597 |
| 12 | 65 | 10.20723 | 51 | 26 | 42.54121 |
| 13 | 64 | 9.444979 | 52 | 25 | 44.18416 |
| 14 | 63 | 8.780627 | 53 | 24 | 46.60972 |
| 15 | 62 | 8.278312 | 54 | 23 | 49.15304 |
| 16 | 61 | 7.885469 | 55 | 22 | 50.96859 |
| 17 | 60 | 7.543627 | 56 | 21 | 53.59359 |
| 18 | 59 | 7.357167 | 57 | 20 | 56.33526 |
| 19 | 58 | 7.258547 | 58 | 19 | 58.34119 |
| 20 | 57 | 7.213675 | 59 | 18 | 61.16667 |
| 21 | 56 | 7.318376 | 60 | 17 | 64.10794 |
| 22 | 55 | 7.459276 | 61 | 16 | 66.32528 |
| 23 | 54 | 7.690442 | 62 | 15 | 69.35324 |
| 24 | 53 | 8.066087 | 63 | 14 | 72.49633 |
| 25 | 52 | 8.40692 | 64 | 13 | 74.94957 |

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| | | | | | |
|---|---|---|---|---|---|
| 26 | 51 | 8.896923 | 65 | 12 | 78.18298 |
| 27 | 50 | 9.526923 | 66 | 11 | 81.53106 |
| 28 | 49 | 10.03951 | 67 | 10 | 84.24849 |
| 29 | 48 | 10.7742 | 68 | 9 | 87.6913 |
| 30 | 47 | 11.64495 | 69 | 8 | 91.24849 |
| 31 | 46 | 12.30988 | 70 | 7 | 94.26264 |
| 32 | 45 | 13.27768 | 71 | 6 | 97.91978 |
| 33 | 44 | 14.37806 | 72 | 5 | 101.6912 |
| 34 | 43 | 15.18284 | 73 | 4 | 105.0393 |
| 35 | 42 | 16.37433 | 74 | 3 | 108.9168 |
| 36 | 41 | 17.69533 | 75 | 2 | 112.9086 |
| 37 | 40 | 18.63308 | 76 | 1 | 116.6334 |
| 38 | 39 | 20.04069 | 77 | 0 | 120.7383 |

If number of patients of type-2 are less than 10 or greater than 31 for fixed number of patients of type-1 and type-4 are 3,20 respectively then the curing capacity of the drug X is not same as that of the drugs Y and Z **(**Fig.1). When r=77-q then that drug X has same curing capacity as that of Y and Z where q=10, 11, 12 ….31 for p=3 and s=20.

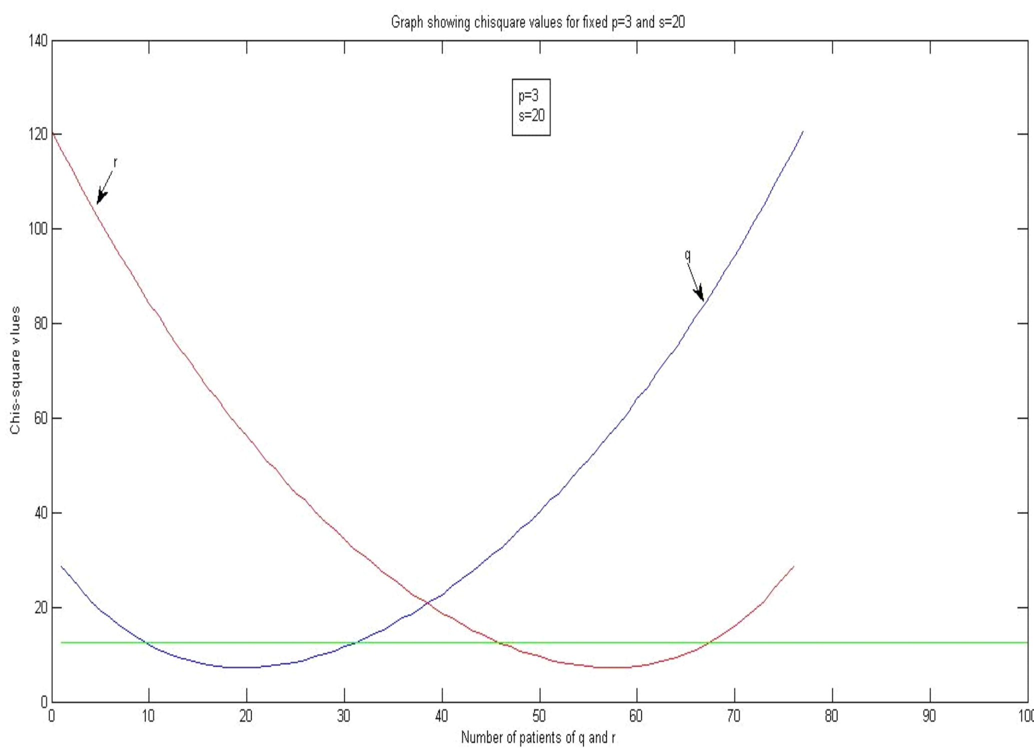


**Fig1.** Graph showing the chi-square values for fixed values of p=3 and s=20

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**Case (ii): Number of patients of type-1 and type-4 are 6 and 24**

If number of patients of type-2 are less than 6 or gresater than 32 for the fixed number of patients of type-1 and type-4 are 6,24 respectively then the curing capacity of the drug X is not same as that of the drugs Y and Z **(**Fig.2). If r=77-q then the drug X is on par with that of drugs Y and Z where q=6,7,8,9,……,30,31,32 for p=6 and s=24.

**Table-2: Table showing q, r and Chi-square values for fixed p=6 and s=24**

| Number of patients | | Chi square value | Number of patients | | Chi square value |
|---|---|---|---|---|---|
| q | r | | q | r | |
| 1 | 69 | 22.810582 | 36 | 34 | 18.199392 |
| 2 | 68 | 20.614153 | 37 | 33 | 19.319781 |
| 3 | 67 | 18.676599 | 38 | 32 | 20.967508 |
| 4 | 66 | 16.021238 | 39 | 31 | 22.855017 |
| 5 | 65 | 14.331728 | 40 | 30 | 24.094746 |
| 6 | 64 | 12.869801 | 41 | 29 | 25.962653 |
| 7 | 63 | 11.061905 | 42 | 28 | 28.118201 |
| 8 | 62 | 9.818519 | 43 | 27 | 29.471754 |
| 9 | 61 | 8.775991 | 44 | 26 | 31.556003 |
| 10 | 60 | 7.612 | 45 | 25 | 33.987791 |
| 11 | 59 | 6.766737 | 46 | 24 | 35.452213 |
| 12 | 58 | 6.5001 | 47 | 23 | 37.750316 |
| 13 | 57 | 5.434437 | 48 | 22 | 40.469444 |
| 14 | 56 | 4.9489 | 49 | 21 | 42.043915 |
| 15 | 55 | 4.624483 | 50 | 20 | 44.554630 |
| 16 | 54 | 4.3512 | 51 | 19 | 47.575234 |
| 17 | 53 | 4.194336 | 52 | 18 | 49.260753 |
| 18 | 52 | 4.186100 | 53 | 17 | 51.984006 |
| 19 | 51 | 4.227407 | 54 | 16 | 55.323459 |
| 20 | 50 | 4.374074 | 55 | 15 | 57.122612 |
| 21 | 49 | 4.662056 | 56 | 14 | 60.059454 |
| 22 | 48 | 4.960242 | 57 | 13 | 63.738639 |
| 23 | 47 | 5.389887 | 58 | 12 | 65.655436 |
| 24 | 46 | 5.959235 | 59 | 11 | 68.808008 |
| 25 | 45 | 6.471296 | 60 | 10 | 72.851673 |
| 26 | 44 | 7.167130 | 61 | 9 | 74.891435 |

| | | | | | |
|---|---|---|---|---|---|
| 27 | 43 | 8.007289 | 62 | 8 | 78.262963 |
| 28 | 42 | 8.701160 | 63 | 7 | 82.700165 |
| 29 | 41 | 9.649488 | 64 | 6 | 84.869456 |
| 30 | 40 | 10.753646 | 65 | 5 | 88.464262 |
| 31 | 39 | 11.605519 | 66 | 4 | 93.328917 |
| 32 | 38 | 12.795242 | 67 | 3 | 95.635512 |
| 33 | 37 | 14.159933 | 68 | 2 | 99.459041 |
| 34 | 36 | 15.152335 | 69 | 1 | 104.790592 |
| 35 | 35 | 16.574557 | 70 | 0 | 107.243482 |

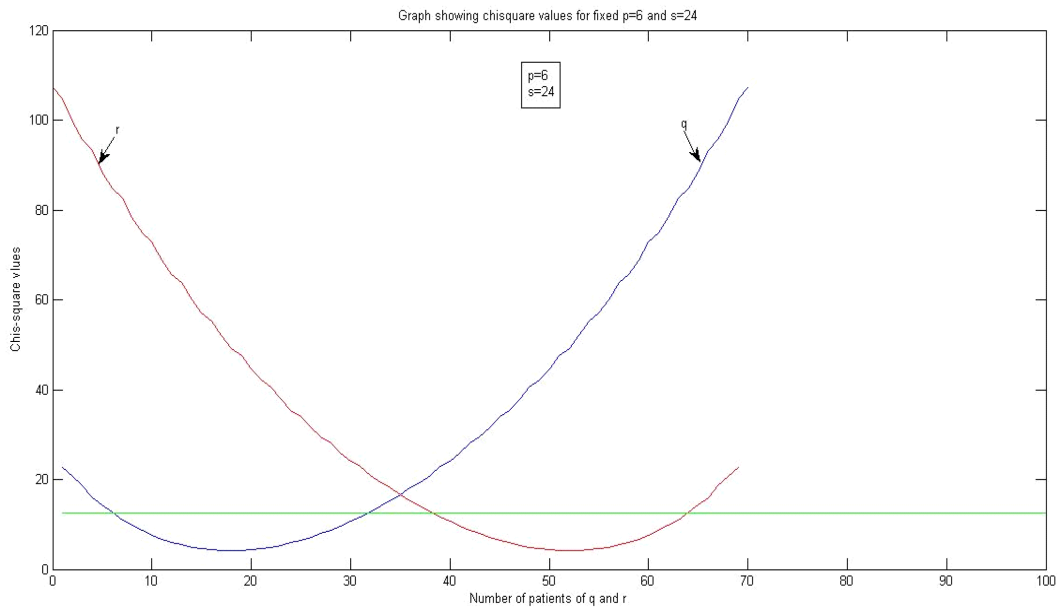


**Fig.2** Graph showing chi-square values for fixed values of p=6 and q=24

**Case (iii): Number of patients of type-1 and type-4 are 17 and 6**

If p=17 and s=6 then the curing capacity of the drug X is not same as that of drug Y and Z for any values of q and r so that q+r =77(Fig.3). We can observe that no value of r and q are below the line parallel to x-axis which represents tabulated Chi-square value. Further **it** is also observed that for any s with p=17 the curing capacity of the drug X is not same as that of other two drugs Y and Z.

**Table-3: Table showing q, r and Chi-square values for fixed p=17 and s=6**

| Number of patients | | Chi square value | Number of patients | | Chi square Value |
|---|---|---|---|---|---|
| q | r | | q | r | |
| 1 | 76 | 52.726190 | 40 | 37 | 46.876190 |
| 2 | 75 | 50.372742 | 41 | 36 | 48.493968 |
| 3 | 74 | 48.220443 | 42 | 35 | 50.236190 |
| 4 | 73 | 45.550414 | 43 | 34 | 51.437146 |
| 5 | 72 | 43.69863 | 44 | 33 | 53.260573 |
| 6 | 71 | 42.036244 | 45 | 32 | 55.206377 |
| 7 | 70 | 40.184524 | 46 | 31 | 56.545097 |
| 8 | 69 | 38.773810 | 47 | 30 | 58.570936 |
| 9 | 68 | 37.541667 | 48 | 29 | 60.717362 |
| 10 | 67 | 36.306494 | 49 | 28 | 62.202381 |
| 11 | 66 | 35.288312 | 50 | 27 | 64.428571 |
| 12 | 65 | 34.439827 | 51 | 26 | 66.773810 |
| 13 | 64 | 33.677579 | 52 | 25 | 68.416757 |
| 14 | 63 | 33.013228 | 53 | 24 | 70.842324 |
| 15 | 62 | 32.510913 | 54 | 23 | 73.385638 |
| 16 | 61 | 32.118070 | 55 | 22 | 75.201190 |
| 17 | 60 | 31.776227 | 56 | 21 | 77.826190 |
| 18 | 59 | 31.589768 | 57 | 20 | 80.567857 |
| 19 | 58 | 31.491148 | 58 | 19 | 82.573792 |
| 20 | 57 | 31.446276 | 59 | 18 | 85.399267 |
| 21 | 56 | 31.550977 | 60 | 17 | 88.340541 |
| 22 | 55 | 31.691877 | 61 | 16 | 90.557879 |
| 23 | 54 | 31.923043 | 62 | 15 | 93.585840 |
| 24 | 53 | 32.298688 | 63 | 14 | 96.728932 |
| 25 | 52 | 32.639524 | 64 | 13 | 99.182169 |
| 26 | 51 | 33.129524 | 65 | 12 | 102.415584 |
| 27 | 50 | 33.759524 | 66 | 11 | 105.763660 |
| 28 | 49 | 34.272109 | 67 | 10 | 108.481092 |
| 29 | 48 | 35.006803 | 68 | 9 | 111.923903 |
| 30 | 47 | 35.877551 | 69 | 8 | 115.481092 |
| 31 | 46 | 36.54248 | 70 | 7 | 118.495238 |
| 32 | 45 | 3.510281 | 71 | 6 | 122.152381 |
| 33 | 44 | 38.610660 | 72 | 5 | 125.923810 |
| 34 | 43 | 39.415444 | 73 | 4 | 129.271942 |
| 35 | 42 | 40.606934 | 74 | 3 | 133.149393 |

| | | | | | |
|---|---|---|---|---|---|
| 36 | 41 | 41.927933 | 75 | 2 | 137.141223 |
| 37 | 40 | 42.865683 | 76 | 1 | 140.86603 |
| 38 | 39 | 44.273292 | 77 | 0 | 144.970867 |
| 39 | 38 | 45.807712 | | | |

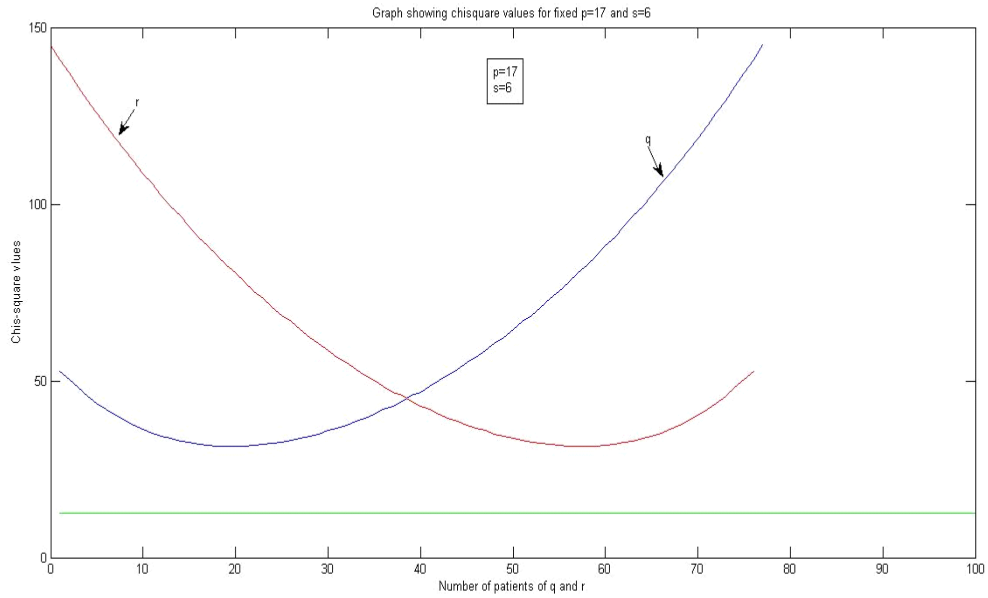


**Fig.3** Graph showing chi-square values for fixed values of p=17 and q=6

**Case (iv): Number of patients of type-1 and type-4 are 20 and 40**

If p=20 and s=40 then the curing capacity of the drug X is not same as that of drug Y and Z for any values of q and r so that q +r =40(Fig.4). We can also observe that no values of r and q are below the line parallel to x-axis which represents tabulated Chi-square value. .

| Number of patients | | Chi square value | Number of patients | | Chi square Value |
|---|---|---|---|---|---|
| q | r | | q | r | |
| 1 | 39 | 36.301647 | 21 | 19 | 37.015229 |
| 2 | 38 | 34.877734 | 22 | 18 | 38.344289 |
| 3 | 37 | 33.704545 | 23 | 17 | 39.815274 |
| 4 | 36 | 31.845144 | 24 | 16 | 41.938756 |
| 5 | 35 | 30.959674 | 25 | 15 | 43.530861 |
| 6 | 34 | 30.343706 | 26 | 14 | 45.317703 |
| 7 | 33 | 29.364935 | 27 | 13 | 47.880221 |
| 8 | 32 | 28.959091 | 28 | 12 | 49.706926 |
| 9 | 31 | 28.852552 | 29 | 11 | 51.799590 |

| | | | | | |
|---|---|---|---|---|---|
| 10 | 30 | 28.552995 | 30 | 10 | 54.814069 |
| 11 | 29 | 28.580902 | 31 | 9 | 56.855556 |
| 12 | 28 | 28.949784 | 32 | 8 | 59.246970 |
| 13 | 27 | 29.186093 | 33 | 7 | 62.732468 |
| 14 | 26 | 29.611688 | 34 | 6 | 64.975663 |
| 15 | 25 | 30.432899 | 35 | 5 | 67.661378 |
| 16 | 24 | 31.101748 | 36 | 4 | 71.643292 |
| 17 | 23 | 31.896583 | 37 | 3 | 74.080526 |
| 18 | 22 | 33.156016 | 38 | 2 | 77.058467 |
| 19 | 21 | 34.182323 | 39 | 1 | 81.568939 |
| 20 | 20 | 35.323990 | 40 | 0 | 84.196970 |

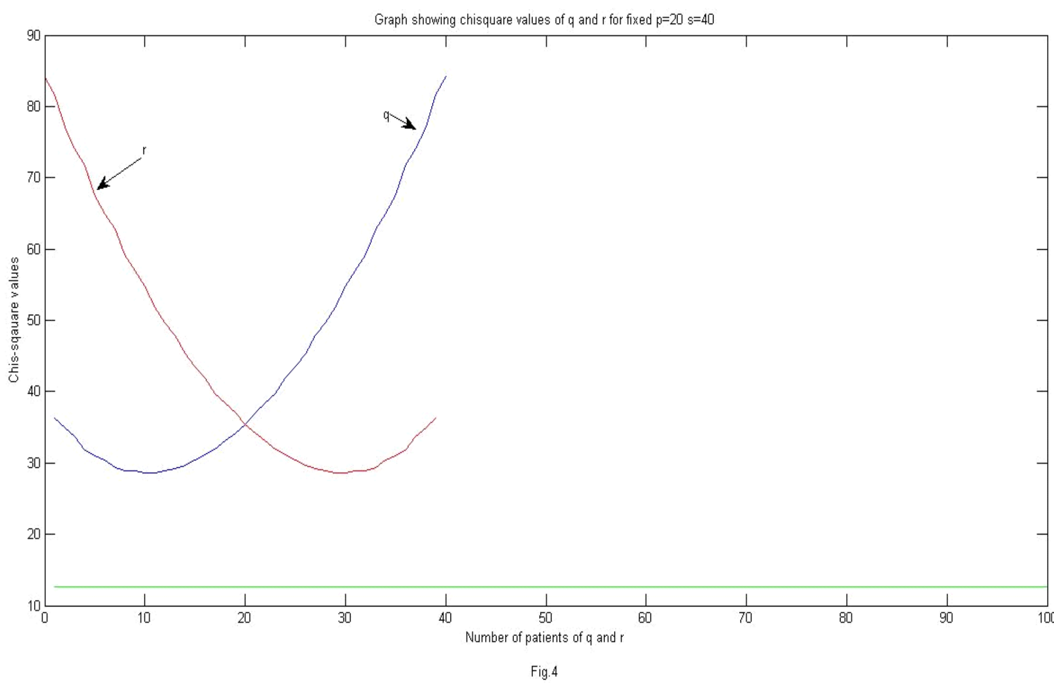


**Fig.4** Graph showing chi-square values for fixed values of p=20 and q=40

**The following is a Matlab program which accept the input values p,q,r,s and gives the output whether the drug is one par with other two medicines/drugs**

```
function result= ksmvalue(x)
po =x(1,1);qo= x(1,2);ro=x(1,3);so=x(1,4);
yo=[2 16 53 29];zo=[7 18 46 29];xo=[po qo ro so];
totxo=sum(xo);totyo=sum(yo);totzo=sum(zo);
for i=1:4
type1sum(i)=xo(i)+yo(i)+zo(i);
end
```

```
gt=totxo+totyo+totzo;xe=round(type1sum*totxo/gt);
ye=round(type1sum*totyo/gt);ze=round(type1sum*totzo/gt);
rowchix2=(xo-xe).^2./xe;rowchiy2=(yo-ye).^2./ye;
rowchiz2=(zo-ze).^2./ze;
chi2xyz=rowchix2+rowchiy2+rowchiz2;
chi2=sum(chi2xyz);
fprintf('chisquare value is %10.4f\n',chi2);
if (chi2<12.59)
   result=1;
  fprintf('x drug is on par with y and z\n');
 else
    result=0;
     fprintf('x drug is not  on par with y and z\n');
 end
```

**Method of execution:**

**Step1**:wite the following at matlab prompt
ksmvalue([ 2 13  35 50])
**Step2:** press enter key
OUTPUT OF THE PROGRAM WILL BE  SHOWN AT MATLAB PROMPT.

**References:**

[1]: Spina, D.,"Statistics in Pharmacology",British Journal of Pharmacology,2007,152(3),pp 291-293.

[2]:Winder, C.V.,"Some examples of the use of Statistics in Pharmacology,1950,Annals of the New York Academy of Sciences.

[3]: Sambaiah,K. et.al. Mathematical modeling for estimation of probability of there being n bacteria at time t in two parameter ,Int. Journal of Innovation in science and mathematics, vol. 3 issue 2, ISSN(on line) 2347-9051(2014).

[4]: James M. Ritter,Lionel D.Lewis, Timothy G.K. Mant, Albert Ferro ,"A text book of clinical Pharmacologym 5th edition 2008, Hoarder Amold, London

[5]: Gupta S.C. and Kapoor  V.K. "Fundamentals of Mathematical Statistics",10th edition, Sultan Chand & sons, New Delhi India.