

Assessing the ratio between new Covid-19 cases and new tests for Sars-Cov-2 in Italy by fractal investigation

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Abstract. Aim: processing the heterogeneous data on the Italian Covid-19 epidemic by fractal investigation on the trend curve of the ratio between new Covid19 cases/new Sars-Cov-2 tests. Methods: New cases of Covid-19 disease and new tests were calculated from raw data freely available on the Italian governing website. The effectiveness of Italian government Decrees aiming to obtain lock-down was assessed by fractal investigation. Self-similarity parameters of presumed fractal shapes obtained 6 days after each Decree were estimated, when possible. Self-organized criticality was also assessed to check for chaos involvement in disturbing the fractal shapes. Shapes were then compared and were used to estimate the number of new tests for Sars-Cov-2 that Italy would be able to perform. Results: The full lock-down changed the biocomplexity of the Covid-19 epidemic in Italy. If the biocomplexity of Covid-19 did not change after the lock-down, Italy should have been able to perform at least 25490 tests daily (± 8940) on average, while real data show that a larger number of tests were done ($p < 0.001$) (thereby obtaining the lowering of contagions). If the same biocomplexity was observed before full lock down, Italy would be able to perform 7088 tests daily (± 5163) on average, while real data show that a lower number of tests were done ($p = 0.029$) (thereby observing the worsening of contagions). Conclusion: in case of heterogeneous data, fractal investigation would be prove useful for assessing and estimating trends. (www.actabiomedica.it)

Key words: Covid-19, Italy, fractal analysis

Introduction

This article has been written in 2020 spring. References and knowledge on the topic refer to the 2020 spring.

Since early December 2019, a new Coronavirus disease was detected in the Chinese city of Wuhan (1). The severe impairment of respiratory function detected in Chinese patients as well as poor knowledge on the new virus behaviour and reports of cases outside the China (2,3) had raised concern worldwide (4). Some countries blocked flights from China, including Italy. However, at the end of February, Italian people received information by media of new cases of the new Coronavirus disease (Covid-19) from two community spread outbreaks in the North of Italy (5). By growing awareness of serious Covid-19 threats in the North

of Italy, the Italian Government promptly decided to limit social contacts to contain contagions (6) until the full lock-down of the country. However, Italy was facing an unknown enemy, with only the previous experience of Wuhan. Under this condition, it was very challenging for the Italian Health System to manage the health crisis, starting from the key point of the data collection (5).

At the beginning of Covid-19 in Italy, authors (7) have reported that Italian data could not be compared with the Chinese data due to heterogeneity. Currently, by viewing the epidemic curves available on the World Health Organization website (<https://covid19.who.int/> accessed 15 May 2020), it can be concluded that the alert was correct, and trends of country epidemics appear to not be comparable. Presumptive variables

that influence the contagious nature of Sars-Cov-2 (8-11) among different population strata mainly involved in the outbreaks (12,13) can explain different trends. However, it can be also hypothesized that there may be biases in data collection worldwide along with different policies of National Health Systems in performing tests for Sars-Cov-2 virus (14).

The aim of the present study is to apply fractal assessment to the Italian epidemic curve of newly diagnosed Covid-19 patients in relation with new tests for Sars Cov-2 disease in Italy. A tool is proposed to monitor the Covid-19 disease amidst heterogeneous data collection, biases and unknown variables influencing the behaviour of contagions.

Methods

At the Italian government site <https://github.com/pcm-dpc/COVID-19/tree/master/schede-riepilogative>, repositories of raw data on Covid-19 outbreaks in Italy since 24 February 2020 are available. Those raw data were updated daily by the Italian task force on Covid-19 disease. Raw data were freely provided as CSV files and PDF files each day, at about the six p.m. (Italian local time) and related to the previous day collection. PDF files were downloaded daily by the author, and data were reported in an Excel file for analysis. The data provided were: number of patients recovered for Covid-19 overall; number of patients recovered in an intensive unit for Covid-19, number of patient with Covid-19 in quarantine, number of overall cases of Covid-19, number of patients discharged from the hospital or healed, number of deaths related to Covid-19, number of Sars-Cov-2 tests performed.

The number of cases of Covid-19 was established by the detection of the Sars-Cov-2 RNA. The specimens were assessed by laboratories displaced from Italian regions and assessed them as determined by government supervision. By increasing of number of outbreaks, more laboratories were able to assess specimens in local hospitals, increasing the number of people able to be tested by time.

The observed delay in the communication of cases and the variable sensitivity of tests for viral RNA collection (15) imply that data are heterogeneous.

Moreover, the Italian National Health System is organized regionally, but, in the same region, Health Units have applied different policies when testing the suspected Covid-19 cases. During the epidemic period, the criteria for specimen collection have been changed. Additionally, it has been reported by media (for example, <https://www.tpi.it/cronaca/morti-coronavirus-dati-istat-10mila-in-piu-rispetto-bollettino-20200423590806/>) that some patients could not have received a diagnosis due to mortality before being tested.

It can be easily understood that those raw data on the Italian Covid-19 outbreak are widely influenced by several variables and biases. For minimizing biases, it was decided to assess the trend of the ratio (R) between new cases of Covid-19 and new tests for Sars-Cov-2, as the variables are obviously linked.

Fractal investigation has already been suggested by several authors (16-19). This type of analysis can describe the complexity of each natural phenomenon. Among those phenomena, the ones involved in biology (biocomplexity) were typically assessed with multivariable models by common statistics. Multivariable models work if independent variables are known and data collection is not biased. However, if unknown variables influence the outcome measure, multivariable models fail or lead to biased results. Even if the data collection is biased, multivariable models should not be performed because they result in biased findings. Unlike multivariable models, fractal analysis of outcome measures in statistics can define the biocomplex phenomenon without assessing single independent variables (16). The premise of fractal investigation is that the same biologic phenomenon occurs in the same time frame but in different places or in the same place but in different time frames. The outcome measures of a common descriptive statistic (e.g., the trend line of R plotted day by day), therefore, could be synthesized as a fractal shape to be compared with other fractal shapes. Change in fractal shapes provides an immediate perception of change in the biocomplexity, suggesting also that one or more variables have changed.

As a second step of fractal investigation, one has to assess how much the chaos is able to disturb or destroy the fractal shape. Chaotic phenomena are common in nature, but nature is also able to self-organize

the phenomenon from chaos (18), providing insight into the assessment of the self-organized criticality during the fractal investigation (16). Therefore, in case of the outbreak of the new Sars-Cov-2 virus, a fractal investigation can be useful for assessing the evolution of the epidemic in spite of biases in data collection and independently from the influence of unknown independent variables.

By retaining a main incubation period of about 6 days (1,20) a change in the shape of R would be observed after 6 to 12 days from each Decree of the Italian government enacted for reducing social contacts. The decrees were enacted on 23 February, 25 February, 1 March, 4 March, 8 March, 11 March, 20 March, 22 March, and 25 March.

According to Glattre & Nygård (16), the first step of the fractal analysis was to estimate the self-similarity parameter α : $\text{Log } F(n) = -\alpha \log(n) + q$ where $F(n) = \sqrt{\{(1/N) * \sum_{k=1}^N [y(R) - y_n(R)]^2\}}$ and $y(R) = \sum_{i=1}^R (R_i - R_{\text{average}})$; $y_n(R)$ is the trend ordered for observation R (the ratio between number of new cases and number of tests). Then, shapes were built and tested for fractality and self-organized criticality. Testing for fractality implies that each segment of the shape (R values of three consecutive dates taken) is able to produce the same clinical shape than the hypothesized fractal shape, as estimated by the aforementioned self-similarity parameter. If not, a certain degree of chaos is considered to be disturbing the fractal shape. For proving if shapes are similar, the difference of self-similarity parameters α (parallelism test of regression lines) are calculated.

The self-organized criticality is checked by proving the fractal shape by performing the Zipf' test and by assessing the level of noise (β coefficient) using the rule $\beta = 2\alpha - 1$ [16].

If the shape is fractal, the Zipf' test is positive (significant test of linearity) and the level of noise is white or pink ($|0 \leq \beta \leq 2|$), then it is assumed that chaos has not disrupted the fractal shape and the outbreak is under control.

In case of self-organized criticality, the formulas reported above can also be used for estimating the number of tests needed to be performed in the same conditions of biocomplexity each day. First, the mean number along with 99.9 confidence intervals of new

Covid-19 cases in fractal segments of the R trend were calculated. Given the mean and the 99.9 confidence interval of the mean, a random sequence of numbers (Open.Epi 3.01 free tool, <http://www.openepi.com/Random/Random.htm> accessed 8 May 2020) of simulated N new cases was generated, which was able to be substituted to the N cases of the fractal segment in correspondence of the full lock down fractal segment (after Mar 25 Decree). Based on the aforementioned rule, the number of new tests for Sars-Cov-2 to be performed each day if the outbreak would have same biocomplexity than the full lock-down period was calculated using the random sequence obtained from mean and 99.9% confidence interval of new cases observed in other phases of the outbreak. Those estimated data were compared to estimated data based on traditional mean and standard deviation values of the real data and with the number of tests really performed.

The calculations of self-similarity parameters (α) and of coefficients of noise (β) were done by using Open-Office 4.1.7. KyPlot 5.0 was used for testing linearity and comparing lines. Additionally, KyPlot 5.0 was used to compare means by using the Student's t test. The significance level of p was set to 0.05. The free software Mandelbulber 2.21 (www.mandelbulber.com) was used for creating fractal images of the outbreak R trend. The same parameters of a default image, except for the self-similarity parameters (α), were set. Additionally, the colors were set to red to depict an increasing R trend and green to depict a decreasing R trend.

Results

For best interpreting the Italian Covid-19 outbreak, information regarding the trends of new cases, new tests for Sars-Cov-2, new deaths (presumably for Covid-19) and new recoveries are provided in Figure 1.

Those trends were provided in \log_{10} scales and describe values from 24 Feb to 30 Apr. Figure 2 reports the trend of R plotted in a Cartesian axis from 24 Feb to 30 Apr.

The biocomplexity of R assessed with the fractal statistic was possible before 23 February, 6 days after 25 Feb, 6 days after 4 Mar, 6 days after 11 Mar and 6

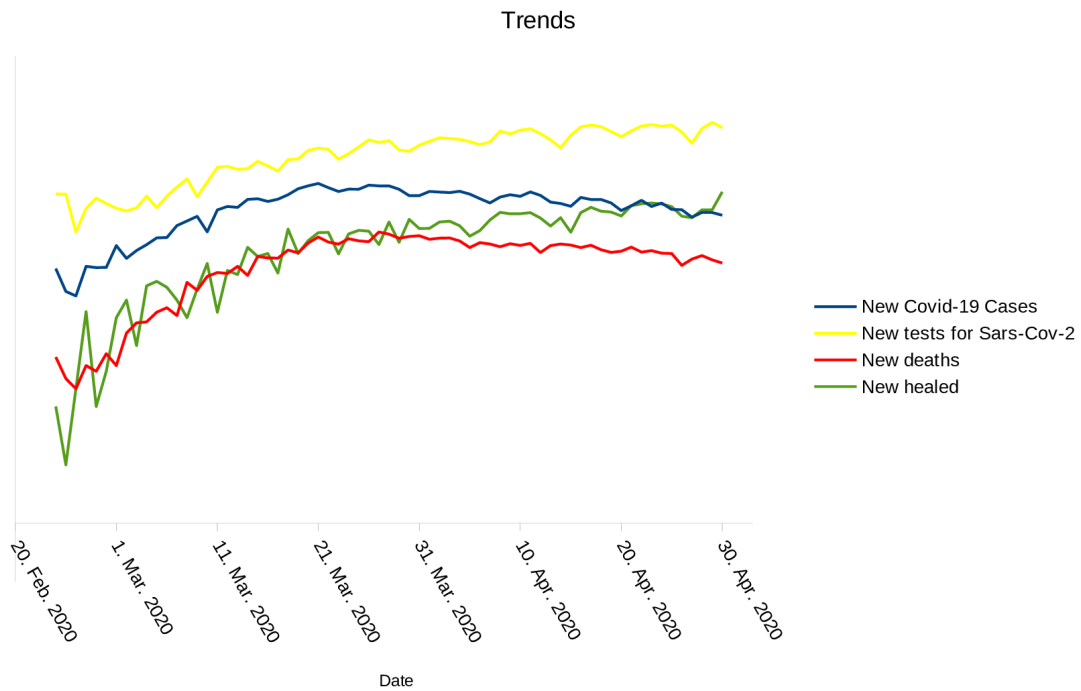


Figure 1. Log₁₀ of Covid-19 epidemic in Italy.

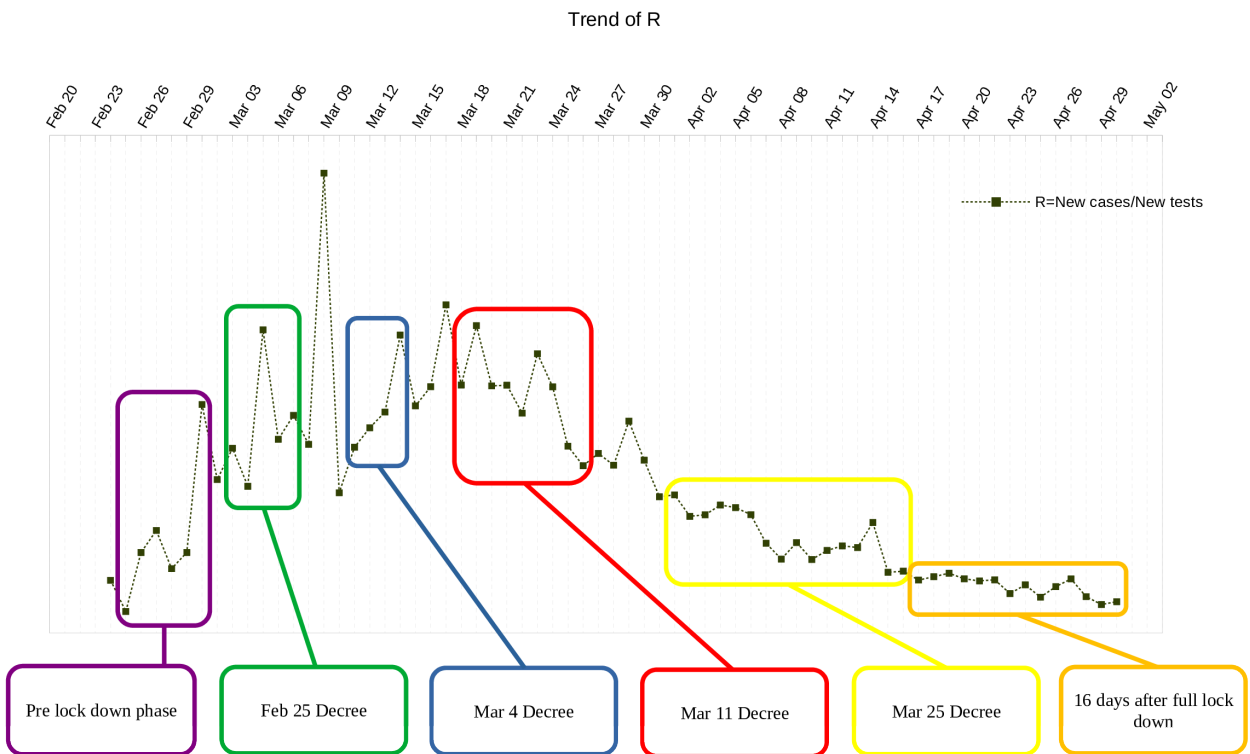


Figure 2. Trend of ratio between new cases of Covid-19 and new tests performed (R). The boxes identify the segments of the trend line where fractal investigation was possible.

days after 25 Mar (until 16 April) (Figure 2, boxes). In other segments of the trend, too few data were available for being assessed. The date of 16 April was chosen arbitrarily, because, after the Easter, Italian citizens could have been less adherent to the full lock-down. After the 3 of May some social activities were started again. A phase of post full lock-down is identified from the 17 of April until to the 30 of April, because data analysis was started the 1st of May.

In Figure 2, boxes of different colors identify the segments of the trend where the fractal statistic was performed. Figure 3 and Figure 4 report the images resulting by using the self-similarity parameters alphas.

A comparison of the results among fractal shapes is reported in Table 1.

The shape after the 4 Mar Decree was not compared with other shapes, because a high level of noise was detected (Figure 3). The full lock-down of Italy

Table 1. Multiple comparisons of shapes

	After Feb 25 Decree	After Mar 4 Decree	After Mar 11 Decree	After Mar 25 Decree	16-days post-lock down
Pre-lock down phase	n.s.	/	0.009	0.001	0.022
After Feb 25 Decree		/	0.017	0.009	n.s.
After Mar 4 Decree			/	/	/
After Mar 11 Decree				n.s.	<0.001
After Mar 25 Decree					<0.001

Legend: p values for comparisons. The shape obtained by analyzing data after the Mar 4 Decree is not compared with other shapes because of high level of noise

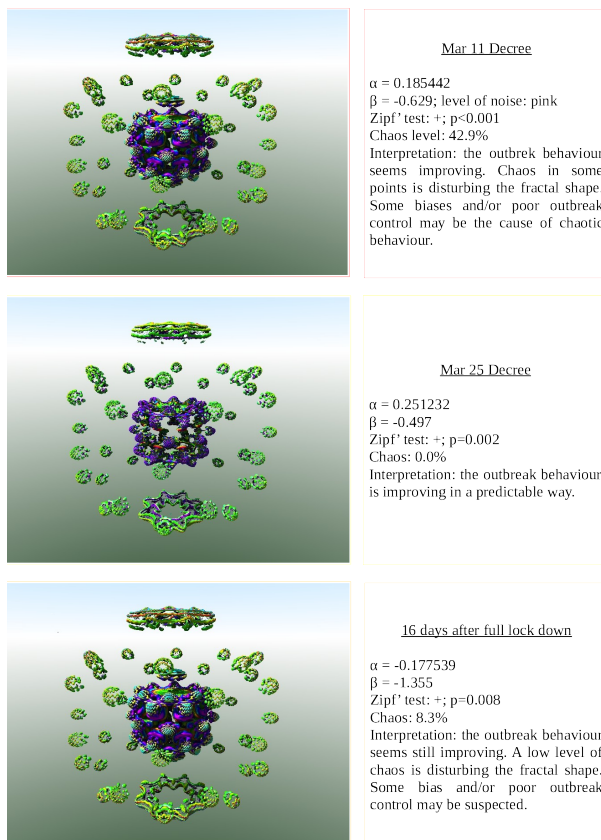


Figure 4. Fractal images of the Covid-19 epidemic: after Mar 11 Decree, after Mar 25 Decree and after 16 days of Mar 25 Decree (16 days after the full lock-down).

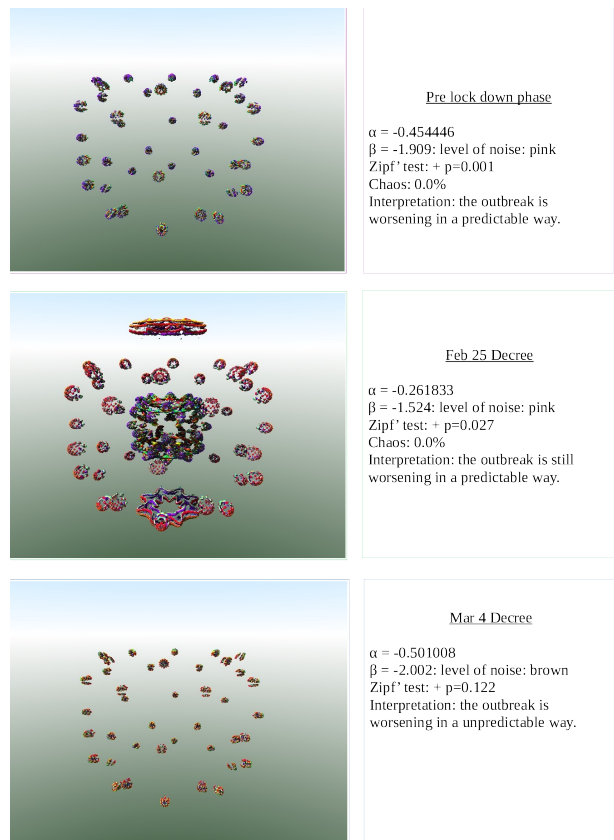


Figure 3. Fractal images of the Covid-19 epidemic: before Feb 23 (pre lockdown phase), after Feb 25 Decree and after Mar 4 Decree.

(obtained with 8 Mar, 11 Mar and 25 Mar Decrees) changed the fractal shape of the epidemic. The post lock-down phase shape is similar to the shapes observed after 25 February and is slightly different than pre lock-down phase.

If the biocomplexity of Covid-19 16 days after the lock-down was not changed, Italy should have been able to perform at least 25490 tests daily (± 8940) on average, while the available data report 57201 tests daily (± 10969). The number is significantly greater than the one estimated ($p < 0.001$). Estimating the number of daily tests by common mean results in 26152 (± 3461), which is not significantly different from the fractal estimate. However, a significant difference was found in the standard deviations among the fractal and common mean estimates ($p < 0.001$ for standardized series).

If, after 25 Feb, the same biocomplexity was observed as after the 25 Mar Decree (under the full lock down condition), Italy would be able to perform 7088 test daily (± 5163) on average, while the available data report 3743 tests daily (± 1319) on average. This difference is significant ($p = 0.029$). The number of tests for Sars-Cov-2 estimated by common mean is 6068 (± 1.511), which is not significantly different from the fractal estimate. Again, standard deviations among two estimates are significantly different ($p < 0.001$ for standardized series).

Discussion

As no sure therapies are administered to Covid-19 patients in Italy, only a full lock-down (6,12,13,21) is able to reduce the spread of Sars-Cov-2. The virulence of the Sars-Cov-2, however, does not seem to be changed with the reduction of social contacts imposed by a lock-down (22). Additionally, the sensitivity of swabs for detecting Sars-Cov-2 RNA is likely low (15); therefore, a robust setting of data was not available to predict the growth of the contagion among usual models for the spread of infectious diseases. If data collection is also not certain (5), each epidemiological model will fail.

Under such a circumstance, testing as many people as possible is a key point for having a reliable pic-

ture of the epidemic. Therefore, the main critical issue becomes how many tests a country is able to perform every day, given a number of new positive patients each day. In that sense, fractal statistics would work better than common estimates based on mean or trends, because the chaotic behaviour of data could be better controlled. This concept is suggested because standard deviations of fractal estimate are larger than the standard deviations calculated by common mean estimate. The higher limit of the standard deviations could be useful to set the lower number of new tests to be performed in case of a full lock-down. Accordingly, real numbers of tests have been lower in the pre lock-down phase (difficulties of testing and isolating new cases, worsening of the outbreak trend) and higher in the post lock-down phase (better policy of tracing and isolating new cases, improving the outbreak trend) than the fractal estimate of number of tests. Additionally, fractal statistics can promptly detect if the outbreak is out of control due to biases or changes in biocomplexity of the epidemic (or both) (as reported in Figures 3 and 4).

Proving the goodness of fractal estimates and behaviour of epidemic would need a prospective assessment, in case of a new outbreak of Covid-19 in Italy, if poor data would be available. Nevertheless, the current article demonstrates that fractals could be prove useful to assess trends amidst poor quality data and can be used as a tool for better managing the spread of infectious diseases under uncertainty.

Conclusion

Fractal investigation estimates could be prove useful for Italy if heterogeneous data will be available in case of new onset of Covid-19, under full lock-down conditions. Accordingly, fractal investigations of trends could be adapted for other countries with same aims.

Conflicts of interest: Author declares that he has no commercial associations (e.g. consultancies, stock ownership, equity interest, patent/licensing arrangement etc.) that might pose a conflict of interest in connection with the submitted article.

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