ADVANTAGES AND DISADVANTAGES OF RT- PCR IN COVID 19

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ABSTRACT:

Coronavirus which is an irresistible sickness was spread overall pandemic. First events of obscure etiology in Wuhan, China. This distinguished a novel coronavirus now named as a SARS COV 2. It is secured by fat protein which is a solitary abandoned RNA genome. The infections are round or pleomorphic with wrapped particles.SARS-COV incites a huge scope starting in China and the new infection is by all accounts infectious and the COVs have become the significant pathogens of developing respiratory maladies. The indications of the beginning periods of the infection are vague. The death rates for cases all around stay between 1% to 2%. Rapid duplication of infections is additionally an entangled factor in identifying the ailment. Consequently the recognition of this sickness can be distinguished by different strategies like RT-PCR (Real time Polymerase Chain Reaction), CT (Computed Tomography) and so forth… RT-PCR is one among them. Detection of infection by RT-PCR in clinical examples offers the alternative of conclusion in the beginning periods of the ailment and its application incorporates genotyping, mutation detection. RT-PCR techniques during the initial hardly any long periods of ailment have been low and much better affectability is after day 6 of the ailment. RT- PCR technique which is found to be a standard method for diagnosing the positive cases. This helps in finding true negativity and rule out the serological positive cases. Thus, this review at the advantages and disadvantages of RT- PCR in COVID 19.

KEYWORDS: Advantages and disadvantages, Coronavirus, Diagnostics, nCOVID 19, RT- PCR technique.

INTRODUCTION:

Coronavirus is an infectious disease. It is the part of SARS family virus which is very much similar for causing respiratory diseases and viral infection and also has major health issues (Pandian, Lalitha Kumari, and Joe 2017). The main target organ is the lungs which may be affected through aerosols and infected droplets (Swetha and Brundha 2017) and it was worldwide spread (Batta et al. 2019)(Mp, Brundha, and Nallaswamy 2019). It is a single stranded RNA virus and the viral genome translated into a large poly protein that is cleaved by viral encoded proteases (Mp, Brundha, and Nallaswamy 2019, Al-Hassany and Al-Jabery 2018). SARS- COV 2 provoked a large scale epidemic beginning in China and the new virus seems to be very contagious (Yarnykh et al. 2016) and the COVs have become the major pathogens of emerging respiratory diseases (Zemlyansky et al. 2017) Rapid multiplication of viru is also a complicated factor in detecting the disease (Peiris et al. 2003). Detection of virus by RT- PCR in clinical specimens offers the option of diagnosis in the early stages of the disease and its application includes genotyping, mutation detection. The clinical sensitivity of the first generation RT- PCR methods during

the first few days of the disease has been low and much better sensitivity is obtained after day 6 of the illness (Wang, Tang, and Wei 2020)(Brundha, Pathmashri, and Sundari 2019). The spread control option is still difficult with no physical contact with other people, being isolated for prolonged duration, difficult with handling household expenses and the people are being neglected for close communication. It is expected that, with this rapid diagnostic method, a prompt identification of this pathogen (Preethikaa and Brundha 2018) will facilitate the control of the disease and the institution of the prompt treatment.

A review with the vital information about the advantages and disadvantages were collected using the recent search engines like PUBMED, GOOGLE SCHOLAR,Core, Cochrane etc., These articles are collected from 2000 to till date. Inclusion criteria includes all the articles related to advantages and disadvantages of RT- PCR in COVID 19. Exclusion criteria includes the articles that are not relevant to advantages and disadvantages of RT- PCR in COVID 19.

PCR in corona diagnosis:

One of the most preferred diagnostic methods used in that PCR (Polymerase Chain Reaction). It was found to be the benchmark in the detection and quantification of RNA targets (Perlman and Netland 2009). It was said to be the gold standard method which helps in diagnosing positive cases of COVID 19. The virus causes first the initial conversion of RNA to DNA template which is the RNA dependent DNA polymerase. The elimination of the post amplification handling helps in reducing the risk of contamination which will turn faster around time and have higher sensitivity (Bustin et al. 2005)(Prashaanthi and Brundha 2018). It also helps in distinguishing the asymptomatic viral shedding and also has sensitivity and specificity (Brundha 2015) of detection. RT- PCR assays for SARS- COV 2 RNA detection were performed using QuantiNOVA probe RT- PCR kit in a light Cycler 48 RT- PCR system. Each 20 microlitre reaction mixture contained 10microlitre of 2x QuantiNOVA probe RT- PCR masterminded, 0.2 microlitre of QN probe RT- Mix. 1.6 microlitre of every 10 microlitre forward and reverse primer, 0.4 micrometer test, 1.2 microlitre of RNase - free water and 5microlitre of TNA as the format. The warm cycling condition was 10 min at 45 degree for the converse transcriptase, 5 min at 95 degree for PCR introductory enactment, 45 patterns of 5 sec at 95 degree and 30s at 55 sec degree Celsius (Corman et al. 2020) (Hannah et al. 2019). Due to other limitations of various methods, RT- PCR remains the most useful laboratory diagnostic test for the COVID 19 worldwide (Shreya and Brundha 2017). It reduces the probability of susceptible and infectious people coming in contact (Ravichandran and Brundha 2016) through early assessment of cases and reduction of contact.

Advantages of RT-PCR:

RT- PCR is a variation of the polymerase Chain Reaction that typically measures RNA expression levels. In RT- PCR, complementary DNA (cDNA) is made by reverse transcribing of the RNA template with the enzymes reverse transcriptase. Viable microorganisms (Ferdioz and Brundha 2016) help in quantifying the virulence with toxin or stress response gene transcription and also in quantifying microbial growth in food matrices. It helps in finding the sensitivity and specificity of detection. PCR which is used for the diagnosis and detection of Bordetella pertussis detect the cross reactivity for Bordetella holmesii (Knorr et al. 2006)(Timothy, Samyuktha, and Brundha 2019). Some of the previous research done with the PCR shows major advantages of using it. The diagnostic accuracy of PCR done in cerebrospinal fluid and also in diagnosis of viral infections of CNS (Persing et al. 2016). Target specificity of PCR assay helps in designing the quantification of taxonomic and functional gene markers and also in the quantification of individual species of phylotypes. Thus, the advantages of RT- PCR is very much helpful in finding many diagnoses in various species.

Disadvantages of RT- PCR:

Also in other hand of detection, the RT- PCR are also having many disadvantages associated with it. Some of the problems associated with this are sensitivity, reproducibility and specificity (Gunson, Collins, and Carman 2006). The long term complication due to rapid multiplication of the virus may give false positive cases and even cancers (Shenoy and Brundha 2016). There is also a problem associated with inadequate availability of samples. The real time PCR in microbial ecology is difficult in detecting the gene and or transcript number, the target specificity in designing of the primers (Smith and Mark Osborn 2009). The fluorescence readings with no template controls (NTC) could be difficult in dye molecule bonding with primers and dimers (Incani et al. 2017, Kumar, Ashok Kumar, and Brundha 2016).

Limitations of PCR in corona diagnosis:

Some of the limitations that are associated with the RT- PCR are that the reaction starts to generate copies of the target sequence exponentially only during the exponential phase of the PCR reaction. RT- PCR may reflect the viral proliferation of clearance in infected patients (Chang et al. 2013)(Brundha and Haritha 2019, Swetha and Brundha 2017, Preethikaa and Brundha 2018). Detection of circulating tumour cells (Balaji, Brundha, and Path 2016) in blood can be done with RT- PCR for carcinoembryonic antigen which was found to be the limitations (Bokadia et al. 2018, Kumar, Ashok Kumar, and Brundha 2016, Maizels et al. 1998). PCR in its different formats helps to detect small amounts of fungal DNA in its raw materials, processed foods (Postollec et al. 2011). Because of inhibitors of the polymerase response found in the sample, reagent confinement, amassing of pyrophosphate particles, and self-tempering of the aggregating item, the PCR response inevitably stops to intensify target grouping at an exponential rate and a "level impact" happens, making the end point measurement of PCR items inconsistent (figure: 1).

Sample collection and maintenances:

Thus , the sample collections are taken from appropriate tissues, fecal samples and the cell lines (Kalaiselvi and Brundha 2016). It was stored in frozen level at 80 degree Celsius and transported in ice i.e dry ice (interstate transport) which is very important for RNA PCR tests and stored at 80 degree Celsius (Smola et al. 2003). Serums that are improved analyses for antibodies, nutrients lipids and lipoproteins, Either serum or plasma are used for proteomic analyses (Vaught and Henderson 2011, Prashaanthi and Brundha 2018). Digital PCR in cell biology is used in genetic engineering and for medical diagnostics are very much portable, low cost, helps in automatic digital PCR systems (Sreejith et al. 2018).

RT- PCR technique:

RT- PCR is the most preferred diagnostic method other than CT and various methods. The gRNA template is converted into complementary DNA (cDNA) by reverse transcriptase enzymes of cDNA (figure: 2). This template is used for exponential amplification using PCR, the QT NASBA is the most sensitive method of RNA detection(Mainar-Jaime, Atashparvar, and Chirino-Trejo 2008). Moreover, isolation of the virus(Harsha and Brundha 2017) requires a biosafety and personal safety level which is not available in most healthcare institutions (figure: 3). Serum and antibody, antigen detection tests have not yet been validated, there may be cross reactivity with SARS- COV which shares a high degree (appx.82%) of nucleotides identified with SARS- COV 2 (Chan et al. 2020). This RT- PCR technique was detected to 520 individual serotype samples for amplifying an appx. 450bp rDNA fragment in second internal transcribed spacer by multilocus genotyping using 10 microsatellites.

Recent advances:

Some of the recent advances with RT-PCR works is that MPCR and PCR - RFLP assays help in routine diagnosis for rapid and specific simultaneous detection of both M. agalactiae and M. bovis (Foddai et al. 2005). RT- PCR helps in replacing the traditional tests and detect fecal viral pathogens in childhood

diarrhoea. Other similar works before nCoV were done for HIV, Mad cow disease, Ebola, flavivirus, Zika virus. Digital PCR in cell biology, genetic engineering , helps in medical diagnostics that are portable with low cost of automatic digital PCR system (Robson and Pain 1971). Some of the alternate methods are to generate antibodies with the spike proteins of the virus and the rapid screening for epidemiological surveillance (Landen 2003).

CONCLUSION :

With this review of the literature, we came to know the advantages and disadvantages of RT- PCR in COVID 19. Thus, this method is very much better in handling and experience to give decreased false positive occurrences of cases. It helps to detect the affected people quickly. Thus RT- PCR paves way for further research and production of better quality diagnostic kit and screening tests.

AUTHORS CONTRIBUTION :

Kameswari.S, contributed to the data acquisition and drafting of manuscript.
Dr.M.P.Brundha, contributed to the design, editing and critical revision of the manuscript. Dr. Ezhilarasan.D, contributed to the supervision and proof reading of the manuscript.

CONFLICT OF INTEREST :

The authors declare no conflict of interest.

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Figure 1: Steps in PCR technique

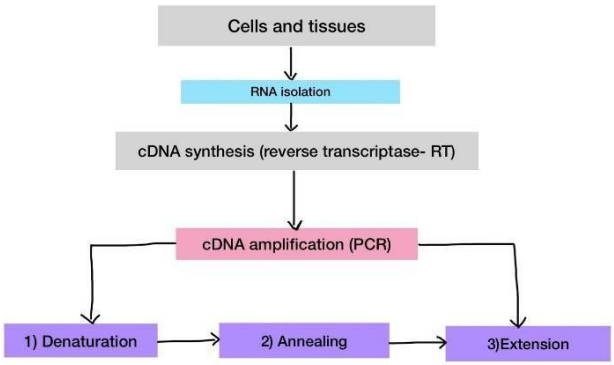

Figure 2: Reverse transcription of PCR

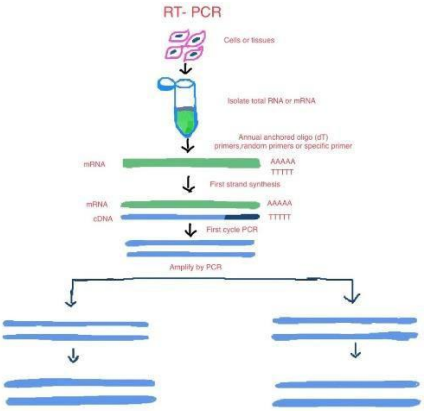

Figure 3: Various works involved in PCR