The Impact of Armed Conflict On The Epidemiological Manifestations of COVID-19 in Libya And Possible BCG Vaccine Induced Protection

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Abstract: The emergence of COVID-19 as a pandemic has a major impact all over the world. Such impacts are rarely studied within countries enfolded by armed conflicts. The objectives of this study were to 1-determine the epidemiological characterization of COVID-19 in Libya 2- The influence of the armed conflict of the geographical clustering of the epidemic 3- Outline the needed policy to control the epidemic and the upcoming consequences. All the officially confirmed cases of COVID-19 were collected from all over Libyan regions from March till Oct.10th, 2020. The data were analyzed and spatiotemporal distribution was determined. The prevalence of the epidemic was determined in each city affected by the ongoing conflict. A total of 41686 cases were reported during the study period. The geographic density varied greatly form one region to another and the war has affected the prevalence within the cities according to their geographic proximity of the ongoing war. The death prevalence from COVID-19 Was estimated at 623/1.5% and was higher among the distant cities compared with the closer cities engulfed in the war. In conclusion our results supports the possible role of timely BCG vaccination in the protection from COVID-19 and more research should be addressed. COVID-19 has great effect on the Libyan community and clearly influenced by the ongoing conflict, Hence then strategies should be planned to combat both the consequences epidemic and the armed conflict.

Key words: COVID -19, Libyan community, Armed conflict, epidemic, BCG

Introduction:

Since its emergence, the novel coronavirus (2019-nCoV) infection has been quickly spreading through all over the world [1]No country can be considered safe, whether rich or poor. COVID-19 is a global concern not only as a huge impact on health services, but also socially, economically and politically [2-4]. Despite that WHO and whole world efforts to fight against this pandemic, some countries were left alone with corona virus and no help was offered.

COVID-19 has also affected most African countries, with over 103,875 cases and 3,184 deaths. The largest number of cases have been recorded in South Africa and 64,388 cases have been reported in the WHO African region reports [5,6].

Libya is the second largest African country which shares its borders with the Mediterranean Sea and possesses huge natural resources. The armed conflict that started in 2011 has continued and became more complicated by April 2019, resulting in extensive mortality, injury and population displacement [7,8].

Armed conflicts cause destruction of infrastructures, physical damage and destruction of healthcare delivery facilities. Hence, conflict zones are more susceptible to the spread of infectious diseases . Concerns about the impact of the pandemic in armed conflict regions have been expressed including Libya, Syria and Yemen, where the impact may go even beyond the borders of these countries [9,10].

The highest rate of mortality was reported in the Syrian conflict (7; 1000) followed by Libya (5; 1000) and Yamen (3; 1000). Such conflicts were complicated by the destruction of health care system, lack of food and unstable daily life [8].

Corona virus have been confirmed in all countries surrounding Syria and full alert has been utilized in Jordan, Iraq and Lebanon, similarly those countries surrounding Libya, (Egypt, Sudan, Chad, Algeria and Tunisia)as well as those surrounding Yemen (Oman and Saudi Arabia [11].

Influx of fighting Militias in Libya from many parts of the world has added extra burdens on the control of emerging infectious diseases in the country including COVID-19[12].

The first suspected cases of corona virus infection in Libya were reported in March 2020. Eight patients arrived from different countries where corona virus infection was officially reported and spread including Egypt (4), Tunis (2), Saudi Arabia (1) and Italy (1)The epidemiological, demographic, clinical and laboratory data, where collected for each patient by direct communications with attending doctors and other healthcare providers.

All patients were treated in isolation and received antiviral, antimicrobial and supportive treatment according to the International Standards . By March 14, 3 (38%) patients had been discharged and 2 (25%) patients had died; all other patients were still in hospital.

In countries like India despite vast population density and growing numbers of COVID19 infections, the mortality rate and severity of COVID has been low in comparison to some TB non-endemic countries (like Europe and USA). In addition, there are evidences that BCG vaccination offers partial protection and survival in low-income countries where tuberculosis is prevalent. The nonspecific effects (NSEs) of immune responses induced by BCG vaccination protect against other infections seem to be due to its immunological memory eliciting lymphocytes response and trained immunity. The protective effect on other viral infection in humans are believed to be mediated by heterologous lymphocyte activation and the initiation of innate immune memory may be applicable to SARS CoV2. A randomized study showed that BCG vaccination prior to influenza vaccination in healthy individuals resulted in a significantly higher antibody response against influenza A (H1N1) compared to

placebo[13]. Prospective clinical trial performed in Japan has shown BCG vaccine to protect from pneumonia in tuberculin negative elderly populations[14]. Miller *et al* [15] correlation between universal BCG vaccination policy) compared number of countries with BCG vaccination policies with the morbidity and mortality for COVID-19. They found that countries without universal policies of BCG vaccination (like Italy, USA) have been more severely affected compared to countries with universal BCG policies. Ozdemir *et al* have shown proportionately less cases, milder illness and a lower death rate in BCG vaccinated population as compared to BCG non-vaccinated across countries and hemispheres[16]. This is so far proven that the countries more prone to be severely affected SARS-CoV-2 didn't adopt universal policies of BCG vaccination like Italy and Spain. The BCG vaccine likely reduces cytokine storm after SARS-COV-2 exposure, resulting mild COVID-19 and early recovery. The immune dysfunction and extent of cytokine overproduction are minimal in children compared to adults.

Methods

The epidemiological data of all confirmed COVID-19 patients from March 25th 2020 to Oct. 20th 2020 in the centers for COVID-19 diagnosis were collected from all the Libyan regions. Data such as the geographic locations and population densities in the counties and regions were collected [17]. Laboratory confirmation of COVID-19 in Libya was done by the National Center for Disease Control. Nasopharyngeal and oropharyngeal swab samples were collected following standard safety procedures. RNA is extracted using QIAamp™ viral RNA mini kit from Qiagen™ according to the manufacturer´s instructions, as previously published [18]. Analysis is done by the real-time reverse transcriptase-polymerase chain reaction (RT-PCR) for all suspected cases following the protocol established by the WHO [19]. Biosafety cabinets are used and the work is done according to laboratory biosafety guidelines.

the prevalence of COVID-19 in each city was recorded along with the distance to the fighting on the front lines. Distant cities were defined as those over 100 km away from the fighting area and adjacent cities as those within 100 km. A map of the regional distribution of COVID-19 from March 25th 2020 to Oct. 20th in Libya was made fig.(1) and the number of confirmed COVID-19 death cases were color coded on the map. Microsoft Excel and SPSS version 12.0 were used for data entry and analysis. Considering the cross-protection reported for BCG vaccination on viral respiratory infections, recent publications have proposed that BCG vaccination could have protective effects against COVID-19 infection .These publications, however, do not include statistical analysis, and the World Health Organization has cautioned about the lack of research regarding BCG vaccination against COVID-19 infection [20]. In view of the growing interest to assess the possible association between BCG vaccination and protection from severe COVID-19, we assessed available global data on BCG and COVID-19 to investigate the hypothesis that countries without a national BCG vaccination program would have greater COVID-19 mortality than countries that have a program, tables (1,2) and fig. (2).

We attempted to control the confounding variables among European Countries and North African Countries such as population density size of the COVID-19 epidemic and number of confirmed deaths / 1million population fig. (3A,3B).

Results

Table 1. Confirmed Covid-19 statistics during the period 25th.March 2020 to 20 Oct.202o for countries with no BCG vaccination policy.

Number	Country	Total cases	Total deaths	Critical cases	Population	Deaths/1 million
1	Austria	394939	7,122	334	9,034,700	758
2	France	2,914,725	70,686	2,813	65,353,232	1,082
3	Italy	2,390,101	82,554	2,544	60,412,645	1,367
4	1sreal	562,167	4,049	1,114	9,197,590	440
5	Portugal	556,503	9,028	664	10,180,248	887
6	Sweden	523,486	10,323	365	10,133,935	1,019
7	1reland	174,843	2,616	199	4,968,055	527
8	Greece	148,925	5,488	322	10,394,834	528
9	Finland	40,505	618	28	5,545,473	111
10	Malta	15,742	241	81	442,192	545

Source(www.Worldometers.info/coronavirus-2020

Number	Country	Total cases	Total deaths	Critical cases	Population	Deaths/1million
1	Libya	109,869	1,698	-	6,922,483	245
2	Algeria	104,092	2,840	42	44,283,520	64
3	Morocco	460,144	7,977	583	37,150,536	215
4	Tunisia	181,885	5,750	385	11,886,516	484
5	Egypt	157,275	8,638	90	103,387,976	84

Table2. confirmed Covid-19 statistics during the period 25th. March2020 to Oct.2020 for north African countries that have fixed BCG vaccination policy. Source
Source(www.Worldometers.info/coronavirus-2020

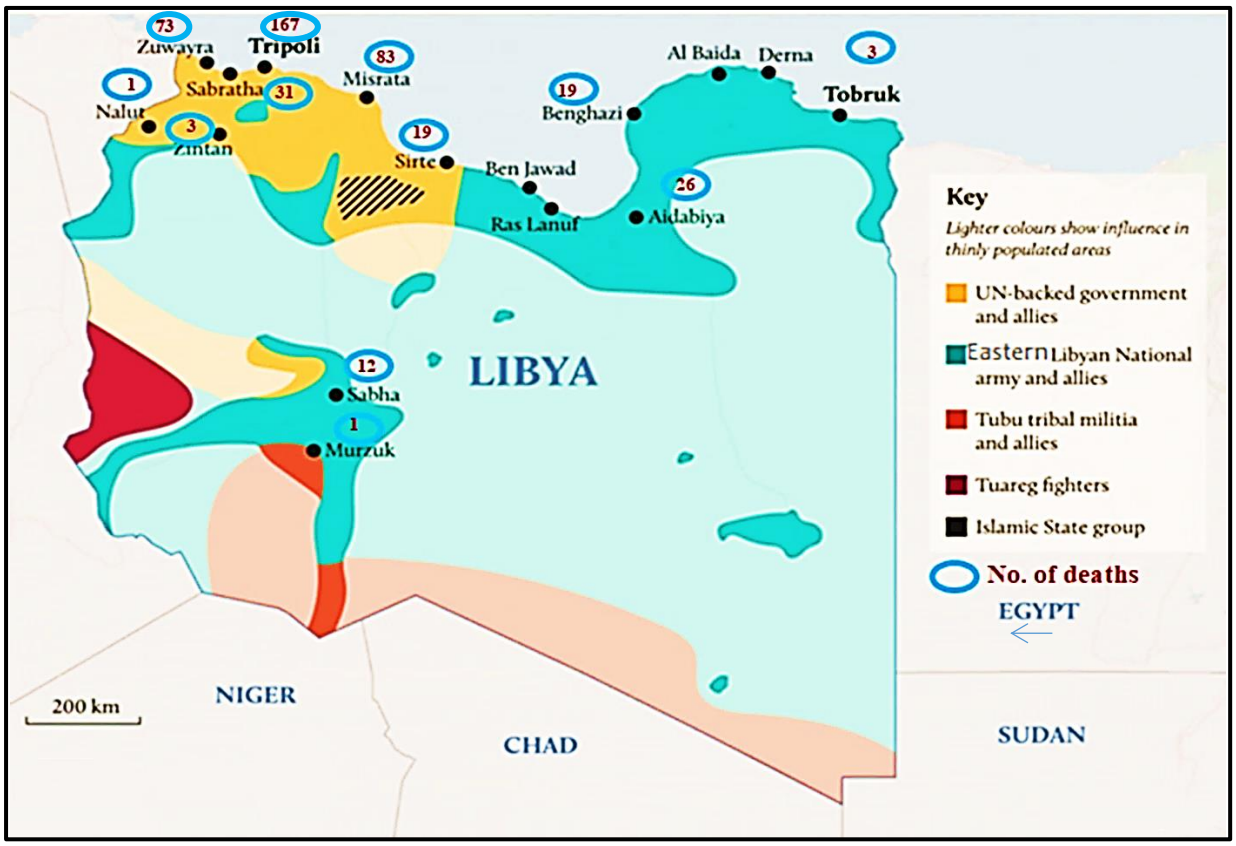


Figure 1: Map of Libya showing the geographic area controlled by each fighting groups during the emergence of COVID-19 and the number of deaths from Covid-19 over the period 12th Oct.2020 To 10th Jan. 2021.

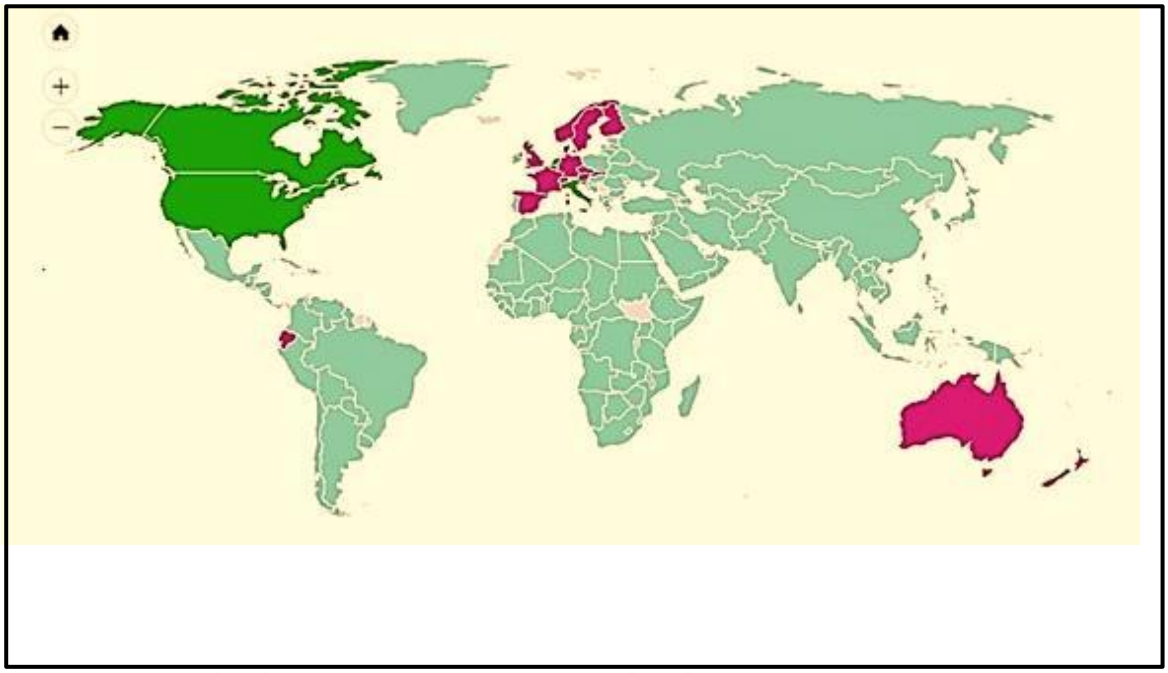
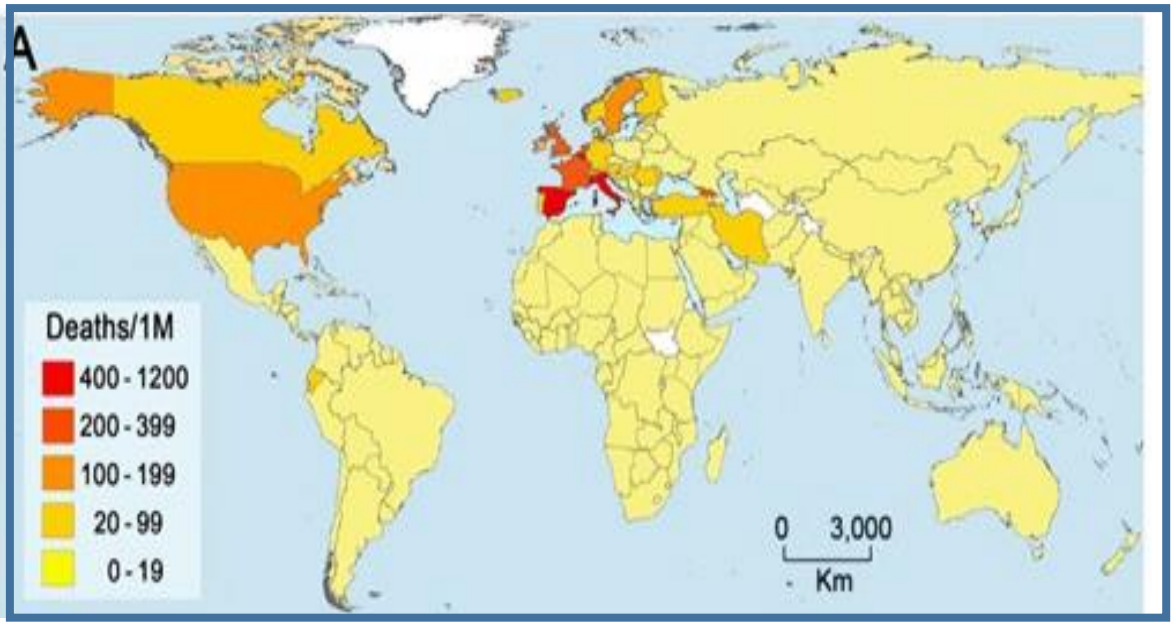


Figure.2. Map displaying BCG vaccination policy by country.
Source(PLoSMed.2020)



Source(PNAS-1019)

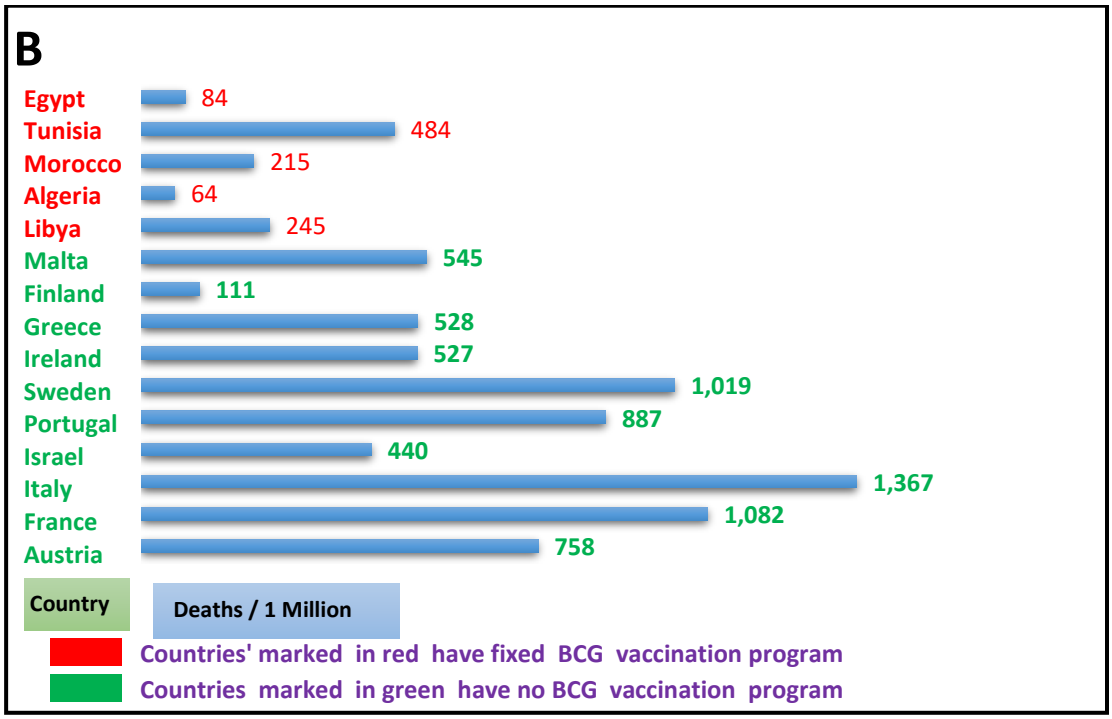


Figure.3(A), (B) Displaying variation in cumulative Covid-19 deaths/ 1 Million for countries adopting national BCG vaccination (North African region) and countries that have no BCG vaccination policy (some European countries) covering the period from the first reported cases up to 19th. Jan. 2021.

Discussion

Based on the 41686 cases reported within a the period 25th. March 2020 - 20th.Oct.2020 we analyzed the epidemiological situation of COVID-19 all over Libyan regions and the effect of the ongoing armed conflict on the pandemic patterns.

This suggests that the epidemic in Libya is not under control and that, strict prevention and control measures have not been adopted in all regions. Nevertheless, despite the numerous challenges that the Libyan population has to face since the armed conflict in 2011 and restarted on April 2019 which continued until 23th.Oct. 2020 where the cease fire was implemented until now. Deaths, injuries and internal displacement of populations; the response to the epidemic and the healthcare system has been reasonable [21,22].

This study investigated the geographic distribution of COVID-19 in Libya and the effect of the ongoing-armed conflict. The number of cases varied greatly from one region to another and the pattern was significantly influenced by the armed conflict.

The armed conflict has affected the geographic spread of COVID-19. The Libyan authorities have taken measures to cut off the source of infection, such as lockdown of cities and implementation of isolation procedures in early stage of the endemic but those were mainly restricted to few cities including Tripoli, Benghazi and western cities. Other regions were not comprehensively or effectively covered. Hence, mapping the disease enables the national authorities to ensure effective implementation of protective infectious disease interventions.

The number of cumulative cases is daily sum of all confirmed cases(death cases) from 25th. March 2020 – 20th. Oct.2020. The regional distribution of COVID-19 was reported as: 167 death cases for Tripoli followed by Misrata (83), Zawya(73), Sabrata(31), Ajdabya (26), Bengasi and Sert (19), Sebha(12) , Zentan and Tobruk (3), Nalut and Murszuk (1).
We visualized the patterns of mortality and injury during the Libyan conflict between 12th.Oct.2020 -10th.Jan.2021. The analysis showed certain districts have been plagued by the conflict for longer period in particular Northern regions (out-districts of Tripoli) where 167 death cases were reported adding to previous war conflict where less number of deaths were recorded naming Bangazi, Derna, Ajdabya and Tobruk fig(1).
The bacillus Calmette-Guérin (BCG) vaccine, an attenuated *Mycobacterium bovis*, has been extensively used in national vaccination programs, as it confers cross-protection from *M. tuberculosis* infection. This epidemiological study assessed the global linkage between BCG vaccination and COVID-19 mortality. Signals of BCG effect on COVID-19 mortality are influenced by social, economic, and demographic differences between countries. Most striking COVID-19 –related deaths are significantly higher in countries with higher quality of life It is possible that people from TB endemic countries like India despite vast population and growing numbers of COVID19 infection, have acquired some protections from severity and deaths from COVID-19 in comparison to TB non-endemic countries (like Europe and USA). Although it appears the immunity may not able to stop COVID 19 infections, but is likely to diminish its impact on severity and mortality.

If the BCG induced protection hypothesis holds true which in our view it will and may have great implications for countries with ongoing national BCG vaccination programs, including most developing countries such as North African countries as they may experience lower morbidity and mortality than some European countries namely France, Italy, Spain and others as shown in fig.2 and fig.3 (A&B). In this study we attempted to compare the number of COVID-19 deaths /1Million for 10 European countries which have no national BCG vaccination programs with five North African countries Libya, Tunisia, Algeria Egypt and Morocco these countries have fixed national BCG vaccination policy Although there are

some differences in the total number of population/1million for the two continents results showed total of 1,092 deaths for North African countries verses a total of 7,294 deaths for the 10 European countries during the study period tables (1) and (2). recent publications have proposed that BCG vaccination could have protective effects against COVID-19 infection [16].

Conclusions

COVID-19 cases and deaths were still increasing in Libya even the ongoing battles has stopped since 23th. Oct.2020, but undetected cases in remote communities in some regions and political unrest may add extra burden on the control of COVID-19 infection. We assessed available global data on BCG and COVID-19 to investigate the hypothesis that countries without a national BCG vaccination program would have greater COVID-19 mortality than countries that have a program. Our results supports the recent investigators finding on the possible BCG induced protection from COVID-19 which we think more clinical trials are needed to recommend the possible use of BCG for the control and prevention of COVID-19 infection not to ignore the impact of the season flue vaccination programs on COVID-19 infection which were implemented in Libya in particular. Establishment of new COVID-19 vaccines which is used by many countries nowadays should bring great hope for the whole international community to get the COVID-19 under control and compact the new emerging variants. The WHO is required to unite all efforts between countries and continents to get the COVID-19 pandemic under control through international corporation.

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