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Epidemiological Characteristics of Poliomyelitis during the 21st Century (2000-2013)

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ABSTRACT

Poliovirus is the pathogenic agent of paralytic poliomyelitis that belongs to the picornaviridae family. Poliomyelitis has an extended history dating over to the Egyptian eighteenth dynasty. It was recognized as distinct disease in the late nineteenth century when the world was ravaged by large number of outbreaks and epidemics in many countries. Paralytic Polio, the rarest but the most severe form of the disease, is characterized by acute flaccid paralysis of any or rarely both of the limbs. Increasing epidemics during the late 19th and 20th centuries lead to the initiation of a worldwide global effort for polio eradication in 1988, super headed by WHO and various other organizations. The launch of Global Polio Eradication Initiative together with the introduction of two polio vaccines resulted in 99% reduction of wild poliovirus cases worldwide while the total number of polio-endemic countries dropped from 24 countries in the year 2000 to only three countries in 2012; Afghanistan, Nigeria and Pakistan. This review will focus on the general biology of poliovirus, some historic and geographic epidemiological aspects of poliomyelitis eradication during the year 2000-2012 and also on the major failing factors associated with the efficiency of the vaccines to eradicate polio in Pakistan.

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1. INTRODUCTION

What is Poliomyelitis?

Developing countries are confronted with a number of destabilizing health problems together with a serious shortage of resources. One such health problem is 'Poliomyelitis' which was first described by Michael Underwood, a physician from Britain, in 1789. He described poliomyelitis as 'the debility of the lower extremities' [1]. Poliomyelitis is derived from two words of Greek origin: polio (that means gray) and myelon (that means marrow, indicating the spinal cord). Thus, poliomyelitis, often called polio or infantile paralysis- a disease of major public health importance- is an acute viral infection that influences the motor neurons within the spinal cord and brain leading to the classic manifestations of paralysis [2].

Early History

Poliomyelitis has a long history, dating back to the Egyptian eighteenth dynasty (1580-1350 BC) [3]. The historical record of polio is very fragmentary and isolated cases of poliomyelitis and acute paralysis in children have been occurring since the biblical times [4]. Regardless of the proof for occurrence of paralytic poliomyelitis was available in the ancient times, it still not distinguished as a distinct disease entity with infectious or epidemic potentialities until the end of 18th century when the epidemics began to appear [5]. Huge number of these epidemics were accompanied by various hysterical reactions [3]. The first epidemics occurred in Europe in the mid-1800s and in North America in the 1890s, after which polio became a global disease with annual epidemics [6]. However, it was not until 20th century that these epidemics became increasingly severe, increasing the number of people affected from the disease in different tropical as well as semi-tropical areas of the world [4] until 1952, when it reached its peak in the United States with over 20,000 paralytic cases [2]. In 1949, John Enders, Thomas Weller, and Frederick Robbins demonstrated that poliovirus brought about visible damage to primate cells derived from tissues other than those of the nervous system. This technology leads to vast- amount generation of standardized poliovirus for vaccine preparation [3]. The introduction of two effective vaccines, killed vaccine (Salk vaccine, inactivated polio vaccine) in 1955 and, eventually, the live poliovirus vaccines (Sabin vaccine, oral polio vaccine) in 1963, were the most important developments made in the history of poliomyelitis [1]. With these two vaccines, providing a one-two punch, polio was down and out for the count at least in the United States, which reported its last case of wild-virus polio in 1979 [2]. Later in 1988, World Health Organization WHO launched a worldwide campaign with an aim to eradicate poliovirus by the year 2005. Though it was not successful, the number of cases has fallen by 99 percent and in 2012; only three countries in the world remained polio-endemic-the lowest count ever- compared to 125 endemic countries in 1988 [7].

Biology of Poliovirus

Causative agent

The infective agent of poliomyelitis has been defined in terms of its source, its pathogenicity and its pathological, histological and immunological characteristics [8]. Poliovirus (PV), the etiological agent of poliomyelitis, was discovered by two Austrian physicians, Karl Landsteiner and Erwin Popper in 1909 [9]. The agent is classified as an enterovirus of the family Picornaviridae, a large family of small RNA viruses and consisting of 9 genera [10],[11]. The virus exists in three serotypes, type 1,2 and 3 (each strain designated by names; Mahoney PV1, Lansing PV2 and Leon PV3 respectively) [12]-[15], on the basis of the four different surface antigenic determinants of the polioviruses referred to as N-Ag 1, 2, 3A and 3B [16],[17]. The polio virion comprise of a single-stranded positive sense RNA molecule encapsidated by an icosahedral capsid which is composed of four proteins VP1, VP2, VP3 and VP4 [18]. Being enteroviruses, they are transient residents of the gastrointestinal tract and thus, are stable at acidic PH but they can be rapidly inactivated by formaldehyde, chlorine, heat, and ultraviolet light [2]. The early evidence clearly indicates that poliomyelitis is a highly contagious infection spread by a close personal contact, mostly via the fecal-oral route and occasionally via oral-oral routes [19],[20]. The human receptor for poliovirus (CD155) is the key for pathogenesis as it is the gate for entry of viral particles into cells [21],[22]. Following infection, the virus replicates in the GI tract and invades the local lymphoid tissues while sometimes; it may cause viremia and invade the central nervous system, destroying the motor neurons and causing flaccid paralysis [18],[23],[24].

Cellular lifecycle of poliovirus

Once the poliovirus gains entrance into the body, it binds to the N-terminal V-type immunoglobulin-like domain of the human poliovirus receptor (hPVR or CD155), a specific cell surface protein present on the intestinal cells of the GI tract [21],[22],[25]. The RNA genome of the virus is released into the cytoplasm of the host intestinal cells via either receptor-mediated endocytosis [26]-[28] or through the pores in the cell membrane formed by myristoylated VP4 and VP1 amphiphatic helix insertion into the cell membranes of the infected cells [25]. Once in the cytoplasm, a cellular phosphodiesterase cleaves a viral protein VPg, which initiates the process of translation of the viral polyprotein through a cap-independent and IRES mediated mechanism, as a result yielding mature structural and non-structural proteins [29]. With the synthesis of the viral proteins, replication of the RNA starts in the cytoplasm of various membranous structures derived from the host endoplasmic reticulum [30],[31]. The viral positive-sense strand serves as a template to promote synthesis of negative-strands by the RNA dependent RNA polymerase. This produces an RNA double-stranded replicative form (RF). The single strand of negative sense RNA molecules then serve as a template

for the synthesis of positive-strand RNA molecules and these new recently synthesized strands either serve as mRNA templates for translation of more viral proteins or targeted for encapsidation in progeny poliovirions [32],[33]. The final steps of the PV lifecycle involve the formation of procapsid and the conversion of the provirion into mature, icosahedral infectious virus particles [34],[35]. Finally, these infectious progeny poliovirions are released through lysis of the infected host cell [36].

Clinical Manifestations

The incubation period of poliomyelitis is around 6 to 20 days with a range from 3 to 35 days [37]. Its clinical manifestations can vary and they are categorized according to severity. Most of the poliovirus infections (upto 95%) cause no illness or are inapparent and asymptomatic infections. Individuals with no clinical symptoms can shed the virus in the stool and thus they are able to transmit the virus particles to healthy individuals. Around 5% of the infections are followed by minor illness without invasion of the central nervous system. These are usually upper respiratory tract infections, GI disturbances and influenza-like illness [38]. 1-2% of the polio infections are non-paralytic aseptic meningitis, recognized by stiff neck, back pain and headache before the onset of paralytic polio. These symptoms last for 2-10 days followed by a complete recovery [6]. A small proportion (0.1 to 1%) is paralytic infections that invade and destroy the motor neurons leading to flaccid paralysis, most commonly affecting the legs and arms [39]. This form, the paralytic poliomyelitis, is the most severe and typical manifestation of the disease. Depending on the extent of CNS damage, they can further be classified into three types: spinal, bulbar and bulbospinal forms [2]. Most patients recover in weeks to months after an acute disease, but residual motor deficits remain in about two-thirds of initially paralyzed patients, some experiencing minor debility while others from permanent, flaccid paralysis [40].

Why target Polio for eradication?

Eradication of most diseases is not presently possible either because there is not an adequate vaccine available or there is an animal or insect reservoir that permits consistent reintroduction of the disease into the human population. However, polio eradication is an achievable goal and there are several reasons to this. First, there is an effective, in expensive and easy to administer polio vaccine [10]. Second, poliovirus have no animal or insect reservoirs as it affects only the human population [41] and third, polio gives long-term immunity and there are no long-term carriers of the disease [42].

Epidemiology of poliomyelitis from year 2000-2012

A striking feature of paralytic poliomyelitis has been its ever-changing epidemiology. Poliomyelitis existed worldwide before the eradication initiative was undertaken in 1988 which marked the launch of the Global Polio Eradication Initiative (GPEI), spearheaded by WHO, Rotary International, the US Centers for Disease Control and Prevention (CDC) and the United Nations Children's Fund (UNICEF) [43]. Overall, since then the number of cases has fallen by over 99% and by 2001,the number of polio-endemic nations dropped from 125 to unequivocally [44].

Year 2000

The annual number of polio cases reported was 719 in the year 2000, which included 24 countries from throughout the world [45]. Following the launch of Polio eradication initiative in 1988, poliovirus transmission was hindered in 18 of the 23 countries of Eastern Mediterranean Region **(EMR)** and was localized to the remaining five. The number of confirmed poliovirus cases reported in EMR countries diminished from 914 in 1999 to 505 in 2000 [46]. Sudan reported only 4 confirmed cases. There was a polio outbreak identified in Mogadishu, Somalia during the year 2000 [47]. Pakistan reported the largest number of polio cases in 2000 i.e. 173 cases, in spite of the fact that the number of confirmed cases declined approximately 40% compared with 1999. It was also widespread in Afghanistan having 27 cases of polio [48]. During the first half of year 2000, there were identified three cases of wild type poliovirus in Upper Egypt [49]. **Iraq** has not detected any case of poliovirus [50]. Year 2000 also reported the first outbreak of vaccine-derived poliovirus (VDPV) type 1 in **America**: three confirmed laboratory poliovirus cases in Haiti and 14 cases in the Dominican Republic were reported [51]. A polio outbreak due to circulating vaccine-derives polioviruses (cVDVP) was documented in **Hispaniola**, a major Island in the Caribbean containing the states of Dominica and Haiti, reporting 22 polio cases [52]. Although considerable advancement has been reported towards interruption of poliovirus transmission in eastern and southern Africa, poliovirus remains

endemic in west and central African countries [53]. Wild poliovirus transmission was reported in central Africa and the Horn of Africa. **African Region (AFR)** incorporates 48 nations and territories and is partitioned geographically into five major epidemiologic blocks: eastern, western, southern, central, and countries in exceptional situations [53]. From among the AFR countries; Nigeria reported 637 cases, 31 confirmed wild poliovirus cases in Congo- Brazzaville, Democratic Republic of Congo (DRC) reported 513 cases while in Ethiopia, there were 144 reported cases [54]. There were a total of 33 cases reported of acute flaccid paralysis (AFP) and seven (21%) deaths, in Cape Verde, an Island in Africa [55]. By 2000, wild poliovirus was discovered in only four of the 10 countries of the South-East Asia Region **(SEAR)**: Bangladesh, Nepal, India and Myanmar. On the whole, SEAR reported 272 confirmed wild poliovirus cases in 2000 in comparison to 1161 cases in 1999 while there were 265 cases in year 2000 reported from India compared to 1126 polio cases in year 1999. Of these 265 confirmed cases, 138 (52%) were poliovirus type 1 (P1), 126 (48%) were poliovirus type 3 (P3) and one polio case was a mixture of P1 and P3. There were 198 virus- confirmed cases in Bangladesh as compared to 393 cases in the year1999. There were two wild poliovirus cases reported from Myanmar (located along the border of Bangladesh) and four poliovirus cases were isolated from Nepal (located along Indian border [56]. There were no indigenous polio cases since the year 1999 in the **European Region**, which comprise of 51 countries. **Western Pacific Region (WPR)** of the world comprises 37 countries and territories and the Regional Commission for the Certification of Poliomyelitis Eradication affirmed it to be polio-free together with China on October 2000 [57]. After the Region of Americas certified as polio-free in 1994, WPR is the second of the six WHO regions to be certified as poliomyelitis-free [58].

During year 2000, advancement towards global polio eradication incorporated a 60% decline in reported poliovirus cases globally within 1 year. While, at the end of 2000, less than 33% of the globe's population lived in countries where polio was endemic, compared with greater than 80% population in year 1988 [59].

Year 2001

Year 2001 reported 483 confirmed poliovirus cases from 15 countries compared to 350,000 cases reported in 1988. These shot up to 1,920 confirmed cases after an outbreak in the Indian states of Uttar Pradesh and Bihar [60].

A total of 91 confirmed cases of polio were reported from five different countries of **EMR** (Egypt, Pakistan, Afghanistan, Somalia, and Sudan) [61]. Pakistan reported 119 polio cases while Afghanistan reported only 11 cases [62]. From 2000 to 2001, the total cases of poliomyelitis increased to 21 in **Haiti and Dominican Republic**. 13 cases of acute flaccid paralysis (AFP) were confirmed in the Dominican Republic, by isolation of type 1 poliovirus while 8 AFP cases were confirmed virologically in Haiti [61]. WHO's strategies for polio eradication in **AFR** caused fast progress in southern and eastern Africa, still transmission of wild poliovirus continued in four important countries: Nigeria, Democratic Republic of Congo (DR Congo), Angola and Ethiopia. There were wild poliovirus cases found in Angola and DR Congo, only 10 cases were reported in Nigeria and wild polio virus was also isolated from a child in Ethiopia[61]. In Year 2001, 31 cases were reported from 4 northern states of Bihar, Haryana, Uttar Pradesh and Delhi in India; and there was no wild poliovirus found elsewhere in any country of **SEAR** [56]. As the epidemic spread into Indian states, the number of polio-infected districts increased from a total of 63 to 159 in year 2001 and because of long border shared by India with Bangladesh and Nepal, these countries were also affected by the polio epidemic [63]. Philippines documented 3 cases of polio outbreak due to vaccine-derived polioviruses cVDVPs [52]. There were no cases of polio reported in the **European region** in the beginning of the year 2001 [57] but during January to March, there were two AFP cases detected in Bulgaria. The total number of AFP cases identified increased rapidly reaching to 33 cases of AFP in November 2001 [64]. The region of **America,** the **Western Pacific region WPR and China,** all reported no cases following the year 2001 [65].

Year 2002

In the year 2002, the number of countries infected from the poliovirus infection reduced from 125 to only 7 countries [60]. 1918 annual cases were reported from these 7 countries n contrast to an evaluated 350 000 cases in 1988 [59]. Together with the Region of **Americas** and the **WPR**, being certified to be free of polio infection in 1994 and 2000 respectively, **European** Region additionally came to be the third WHO region certified as polio-free in 2002 [58],[59]. There was a significant rise in poliovirus cases from 483 in 2001 to 1,920 polio cases in 2002 [59]. Considerable advancement has been made in the **EMR** nations in the midst of 2002 [66]. Few cases were reported from Afghanistan (11 cases), 7 cases detected from Upper Egypt during the second half of 2002, while Pakistan reported 22% lesser polio cases in 2002 (93 cases) as

compared to year 2001 (119 cases). There were zero cases of polio reported from Sudan. In the **AFR** countries, there were no cases reported from Ethiopia and Angola [59]. There were three virologically confirmed polio cases indentified in Somalia while it reported the last polio case in October 2002 [67] (28), 3 cases from Niger and an outbreak of circulating vaccine-derived poliovirus cVDVP was detected in year 2002 in Madagascar [59]. Despite a substantial progress in the **SEAR** countries, poliovirus transmission continued during 2002 in northern India [68]. A four-fold increase in polio incidence globally, focused mainly on India and northern Nigeria [59]. In India, there was a drastic increase in polio cases reported in 2002. The polio cases built from 268 in year 2001 to 1,599 polio cases in 2002; of the aforementioned, 59% were in squirts from Muslim groups, which represent more or less 20% of the total Indian population (69). 1,363 (85%) of the cases reported from India were identified in areas of Uttar Pradesh and Bihar and 49 in West Bengal [70]. Nigeria reported 201 polio cases [59]. There were no wild poliovirus cases identified in Nepal and Bangladesh [71].

All endemic countries with the exception of Somalia continued to report increasing wild poliovirus cases in year 2003.

Year 2003

Rumors concerning the safety of polio vaccine in year 2003, and consequent refusal of vaccine use in Nigeria, headed to a build in cases and spread of the virus to surrounding polio-free countries [72]. In 2003, there were only 784 confirmed cases of polio globally, and polio remained endemic in six countries worldwide [73]. These six endemic countries include Nigeria, Niger, Pakistan, India, Afghanistan and Egypt [74]. In 2003, there were 51 cases of polio reported from eight countries in West and Central Africa that were previously polio-free. In **Pakistan**, reported polio cases expanded from 90 in year 2002 to 103 in 2003. **India**, the just remaining SEAR country with progressing indigenous transmission of WPV, made major advancement in 2003 for polio destruction [70]. India reported 225 wild poliovirus (WPV) cases, which marked a significant decline from a global total of 1,600 cases reported in 2002. Of the total 225 polio cases, 203 cases (90%) were type 1 WPV (P1), and 22 (10%) were type 3 WPV (P3). Out of 225 total cases, 88 were reported in Uttar Pradesh, 18 in Bihar, and 28 in West Bengal [70]. **Nigeria**, the most populated African country reported a total number of 355 wild poliovirus (WPV) cases in 2003, making up for 45% of globally reported cases and >80% of cases reported from the African Region (AFR). Of the reported 355 WPV cases, 192 were PV type 1, and 163 were PV type 3 [75]. **Egypt** recorded one polio case in contrast to seven cases reported in year 2002. The number of cases identified in **Niger**, which fringes Nigeria, expanded from 3 polio cases in 2002 to 40 cases in year 2003 while **Afghanistan**, sharing a cross-border reservoir of progressing poliovirus transmission with Pakistan, reported 8 polio cases in the year 2003 [69].

World was never so near to success, with just six countries remaining free of polio infection. Thus, in 2004, the world has its best chance to stop polio forever.

Year 2004

In 2004, importation of wild poliovirus caused re-infection in countries that had previously interrupted transmission. This increased the number of cases to 1,263 in 18 countries [76].

The African Region (**AFR)** countries reported a total of 728 confirmed poliovirus cases in year 2004 [77], out of which 12 confirmed wild-poliovirus cases were reported in Niger while Nigeria reported 133 cases of wild poliovirus [69]. The countries in Eastern Mediterranean Region (**EMR)** reported 54 polio cases altogether. Afghanistan reported only two poliovirus cases [69], one case was reported from Egypt and 12 wild poliovirus cases from Pakistan [78]. India, the only polio-endemic **SEAR** country, reported 134 cases in 2004, historically the lowest ever, most of which were from western Uttar Pradesh and Bihar [79]. Also in year 2004, the **Western Pacific** Region WPR, the **European Region** and the region of **America** remained polio-free, reporting zero cases of polio [78]. There was an outbreak of vaccine-derived poliovirus (cVDVP) documented in **China** in year 2004 reporting two polio cases [80].

Year 2005

In year 2005, the world has moved quite a lot milestones close to polio eradication, together with the success of introducing new monovalent oral polio vaccines [81]. Since year 1988, the efforts of global polio eradication have decreased the number of polio cases by nearly 99%, i.e. from 350,000 per year to 1,469 cases in 2005 [82]. There were only 4 countries remaining with endemic polio: India, Pakistan, Afghanistan and Nigeria. The last poliovirus in Egypt was isolated from an environmental sample in January 2005 [83], and nine polio cases reported in **Niger** were all the due to importations over its' heavily- traveled border with

Nigeria. On the other hand, **Nigeria** reported 830 wild poliovirus cases [84]. Ten countries, which have been re-infected with poliovirus, include: Chad, Yemen, Somalia, Angola, Sudan, Ethiopia, Cameroon, Indonesia, Eritrea and Mali. There were 1,000 polio cases (54% of the cases reported globally) from these countries with several outbreaks initiated by importations [85]. Since the disease surveillance started in 1996, Yemen became free of any polio infection. In year 2005, Yemen identified 478 poliovirus cases in the country, 185 cases were reported from Somalia [83] and Sudan reported 24 confirmed wild poliovirus cases. There were 22 cases reported in various districts of **Ethiopia** in 2005 [86]. Indonesia had not reported any case of polio since 1995. The country's largest-ever recorded outbreak of vaccine-derived type 1 poliovirus (cVDVP) was documented in central Java, Sumatra and Jakarta parts of **Indonesia** reporting 225 polio cases [87]. The high disease burden in Indonesia raises a concern of potential spread of poliovirus across Asia, including countries such as Philippines, Malaysia and China. There were two large polio-endemic Asian countries which accounted for 50% reduction in cases from year 2004 to 2005 [83]. Altogether, the number of poliovirus cases in **India** and **Pakistan** in the final quarter of 2005 fell by more than half compared with the past year, reason being the more effective immunization procedures and adequate use of monovalent polio vaccine [88]. Pakistan reported 28 poliovirus cases in year 2005. Out of these 28 cases, all polio cases were WPV type1 except one case that was WPV type 3 (identified from Quetta district Baluchistan province) [89]. India, a highly populated and a polio-endemic SEAR country, intensified polio destruction efforts by introducing extra surveillance and immunization procedures together with introducing monovalent oral poliovirus vaccine for types 1 and 3. The reported cases reduced from 134 in 2004 to 66 in year 2005 [90]. India was the only polio-endemic country of SEAR in 2005 while **Nepal** also reported 4 wild poliovirus cases in this year. Bangladesh remained polio-free throughout the year 2005. **Afghanistan** reported a total of nine wild poliovirus cases in year 2005[83].

Year 2006

By year 2006, there were lesser than 2,000 polio cases reported all around the world—a decrease of >99% from year 1988—and polio was now endemic in only four countries worldwide [10]. These four countries include: Afghanistan, India, Nigeria, and Pakistan [87]. 6% of the total cases in 2006 were from the nine other countries with importations of poliovirus [91]. From among the EMR countries, **Iran** reported 107 polio cases in 2006 [92]. In **Pakistan**, an increase in poliovirus cases was observed from 28 cases, isolated from 17 districts in 2005 to 40 cases from 20 districts in 2006. However, approximately 80% of districts of Pakistan were polio-free in 2006 [93]. In the same year, the Afghanistan and Nigeria reported the highest number of cases compared to a sum total of cases in the past six years, while the total polio cases in India were higher than the cases reported in any of the previous four years [73]. Most of **Afghanistan**, another EMR country, remains without any polio infection, with the exception of continuous transmission in the Southern Region. 31 cases were reported in 2006, in contrast to 9 polio cases in year 2005 [93]. Among the SEAR countries, an outbreak of polio in Uttar Pradesh reintroduced poliovirus in various **India** territories that were previously free of polio giving 10 times rise in polio cases in year 2006 as compared to year 2005 (i.e. 676 polio cases versus 66 cases respectively) [94]. Since year 2000, **Bangladesh** reported its first polio case in Chandur district in Chittagong and by the end of year 2006, the total poliovirus cases added upto 18 cases from the country [95] while there were 5 cases of wild poliovirus reported from Nepal [96]. In year 2006, **Nigeria** reported 1,123 wild poliovirus cases, in contrast to 830 polio cases in year 2005. Approximately 60% of the total wild poliovirus cases were reported from three states of northern Nigeria (Kano, Katsina and Jigawa). There was an outbreak of 22 cases of cVDVP reported in Nigeria in this year [93] . In 2006 Niger and Egypt pass one year without any polio cases [85]. **Namibia**, an AFR country, has detected no wild poliovirus (WPV) transmission for ten years until fire-back of poliomyelitis cases in 2006, subsequently due to importation of wild poliovirus type 1 (WPV1) from neighboring Angola. It made up to 19 cases of poliomyelitis [97]. Other nine non-endemic countries reported a total of 128 wild poliovirus cases in the year 2006 [98].

Year 2007

27 polio-free countries were re-infected with imported poliovirus between 2003 and 2007. 20 of the total re-infected countries were a result of the virus that originated from northern Nigeria [95]. The other six countries include, Angola (9 cases), Chad (6 cases), Democratic Republic of Congo (32 cases), Niger (209 cases), Myanmar (11 cases) and Somalia, [99].

A global total of 1,315 cases were reported in the year 2007. Among the four countries that have never interrupted poliovirus transmission, Nigeria is one them while the others being India, Pakistan and Afghanistan [100].

In year 2007, 353 wild poliovirus cases were reported in **Nigeria**. The first case of wild poliovirus 3 (WPV 3) since 2004 was also reported from Southern Nigeria in 2007 [100]. And also an outbreak of 71 cases of cVDVP was reported from Nigeria. In 2007, constrained advancement occurred towards interrupting wild poliovirus infection and transmission in the **EMR** countries: Afghanistan and Pakistan. **Pakistan** observed decline in total number of confirmed poliovirus cases from 40 (reported from 22 districts) in 2006 to 32 cases (reported from 18 districts) in 2007. While, in the same year, **Afghanistan** reported 17 confirmed poliovirus cases, (from 13 districts), compared to a total of 31 cases (from 17 districts) in the previous year [101]. In March 2007, **Somalia** became polio-free EMR country after reporting its last case of polio in Mudug province, in central Somalia [102]. Iran, in 2007, reported a total of 58 polio cases [50]. **India** was the only SEAR country that remained polio endemic reporting 894 wild poliovirus cases in 2007[103].

Year 2008

The year 2008 proved to be a turning point in the fight against polio. 1,652 wild poliovirus (WPV) cases were calculated worldwide in 18 countries of the world, which represents an increase of 26% compared to 2007. 976 cases were wild poliovirus type 1 (WPV1), 675 cases were wild poliovirus type 3 (WPV3) and one case was a mixture of wild poliovirus type 1 and 3 [104].

91% of all polio cases occurred in the four previously polio-endemic countries: Nigeria, Pakistan, India and Afghanistan [105]. **Nigeria,** the only polio-exporting country in the world, poses the single biggest threat to the global eradication of polio [104]. The number of cases nearly tripled in 2008, in Nigeria, due to a rise in type 1 polio reporting a sum total of 801 wild poliovirus cases [105]. In year 2008, western Uttar Pradesh – a globally established reservoir of wild poliovirus in **India**, stopped the transmission of indigenous type 1 poliovirus bringing type 1 to the verge of eradication in both Uttar Pradesh and Bihar states. However, there were 559 polio cases reported in 2008 in India due to a large outbreak of type 3 WPV in central Bihar and western Uttar Pradesh [104],[105]. **Nepal** also reported six cases of poliovirus due to single importations from either Bihar or Uttar Pradesh. Inspite of intense actions taken to eradicate polio in Afghanistan and Pakistan, transmission of wild poliovirus expanded in **Pakistan** and as held on in the southern region of Afghanistan [104]. Pakistan reported a total of 118 wild poliovirus cases in 2008 while **Afghanistan** reported 31 cases only. In 2008, 14 countries had circulation of imported poliovirus. Of these, 10 countries were infected by WPV of Nigerian origin and four by WPV of Indian origin. These countries reported a total of 146 cases of imported wild poliovirus [105]. Along with Nigeria, the other **AFR** countries reporting wild poliovirus cases in 2008 include: Sudan**,** recording 26 poliovirus cases, Ethiopia reported three cases of polio on its border with southern Sudan, DRC and Angola also identified few cases . Chad, in central Africa reported the highest number of cases compared to any African country [104].

Vaccine-derived polioviruses (VDPVs) type 2 was identified in year 2008 from the AFP cases from seven countries. 148 cases were indentified in northern Nigeria, 2 cases from Ethiopia and there were two individual outbreaks of 2 and 11 cases of type 2 cVDVPs in DR Congo [106].

Year 2009

Importations of wild poliovirus in year 2009-2010 lead to re-infection of 23 previously polio-free countries of the world [43]. Global total of 1,606 cases of wild poliovirus infection occurred in contrast to 1,651 cases in the previous year, 2008. Incidence of wild poliovirus type 3 in 2009 increased by 67% while that of wild poliovirus decreased 51 % [107].

From among the four polio-infected countries of the world, **India** was a country where highest numbers of polio cases were reported in 2009 affecting 56 districts of India. There were 741 wild poliovirus cases reported [108]. 89 polio cases (60 WPV1, 28 WPV3, and one mixed WPV1/WPV3) were reported from **Pakistan** in 2009 while it's neighboring county, **Afghanistan** reported 38 wild poliovirus cases in the same year; 15 WPV type 1 and 23 WPV type 3), compared with a total of 31 wild poliovirus cases in 2008 [107]. In **Nigeria,** polio cases fell from 798 in 2008 to 388 in year 2009. As a consequence of importations carried out in the year 2008, wild poliovirus transmission was re-established in Angola and Chad as well as in DR Congo and southern Sudan. The imported poliovirus caused a total of 178 cases in 2009. WPV type 1 outbreaks in Kenya and Uganda in 2009 also occurred as a result of importations from southern Sudan. In 2009, there were 175 cases of circulating vaccine-derived polioviruses (cVDPVs), reported from six countries: 153 cases from Nigeria, one case from Guinea, 4 cases from DR Congo, two cases from Ethiopia, 4 cases from Somalia and 11 cases from India [107].

Year 2010

In year 2010, the Global Polio Eradication Initiative (GPEI) incorporated new techniques for checking advancement and specific mechanisms for taking curative steps, in order to interrupting poliovirus transmission by the finish of year 2012 [107]. Polio cases have diminished by over 99% since the launch of GPEI in year 1988, from an approximate of 350 000 cases across more than 125 endemic countries to around 1352 reported cases in year 2010 [43]. All the four polio- endemic countries (Nigeria, Afghanistan, Pakistan and India) observed a substantial fall in the reported cases of wild poliovirus in the year 2010 except Pakistan. **Pakistan** had the worst indicators of children affected from the disease in 2010 in comparison to other countries [98]. It's polio cases increased from 86 in 2009 to 140 in 2010 [89] . During the years 2010 and 2011, **India** made substantial advancement towards polio destruction, recording 94% decline in polio cases, thus giving the country a great opportunity to annihilate the disabling disease [98]. Contrasted with a total of 741 cases of polio in 2009, India recorded only 42 cases in year 2010, 18 cases were reported to be from WPV type 1 and 24 cases from WPV type 3 [109]. India also reported 21 cases of circulating VDPVs in the following year [110], while in **Nigeria** there were 388 cases in 2009, which decreased to 21 wild poliovirus cases in 2010 [99]. WPV type1 huge outbreak occurred in following year in the **European region**, a region declared to be polio-free in 2002 and no poliovirus cases were reported since then until 2010, when the first wild poliovirus importation was done into the European Region. This resulted in 476 confirm wild poliovirus cases: 14 cases in Russia, 458 cases in Tajikistan, 3 in Turkmenistan, and one in Kazakhstan. 19 importations of WPV type1 and 11 imports of WPV type 3 took place during 2008-2009 resulting in 208 poliovirus cases in 15 countries of the world in year 2009 and 7 extra cases in year 2010 [111]. There were seven importations of wild poliovirus type 1 and two importations of wild poliovirus type 3 that resulted in overall 26 poliovirus cases in 4 **African countries**. In Angola, there were 33 WPV confirmed cases reported in 2010, in Chad there were 26 cases due to importations from Nigeria while in the Democratic Republic of Congo (DRC), around 100 WPV cases were identified [99]. In 2010, as a result of poliovirus importations, there were two outbreaks observed in the Asian countries of Nepal and Tjikistan. In Nepal, five WPV type 1 (WPV 1) cases were identified followed by two separate importations while in Tajikistan, 452 WPV1 cases were confirmed in 2010 [112]. Additional wild poliovirus type 1 (WPV1) case was confirmed in 2010 in Pointe Noire, a resident of the port city. This was the first wild poliovirus case in 10 years reported from Republic of the Congo (ROC) [109]. In year 2010, cVDVP type 2 cases were indentified; 27 cases in Nigeria, 18 cases in DRC, 2 cases in India and 5 cases in Afghanistan were reported. Ethiopia also reported 6 cases of cVDVP type 3 [110].

Year 2011

Global total of confirmed cases of polio reported comprehensively diminished by 52% (i.e from 1,352 cases in 2010 to 650 cases in 2011). From the mentioned 650 cases of year 2011, includes 341 (53%) cases from the four polio-endemic countries i.e. Nigeria, Afghanistan, Pakistan and India, 230 (35%) cases from the countries that were previously free of polio i.e. Chad, Angola, and Democratic Republic of the Congo DRC), and 79 (12%) cases were identified from nine countries affected by the huge outbreaks of polio [98].

In comparison with year 2010, there was a rise of wild poliovirus cases in year 2011, observed in Afghanistan (69%), Nigeria (66%), and Pakistan (27%), but in India, the cases fell by 98%(98). **India,** the only SEAR polio-endemic country left, reported last case of poliomyelitis on 13 January 2011 in a two-year-old girl in West Bengal [98]. There were no cases of WPV reported in India since January 2011, but, despite this, the hazard for WPV circulation remained in the high-risk areas in central Bihar and western Uttar Pradesh [109]. India is no longer polio-endemic, leaving behind the three countries: Afghanistan, Pakistan and Nigeria, which have never stopped polio. For year 2011, **Pakistan** experienced the third highest number of reported cases across the globe, behind Chad and Democratic Republic of Congo. There were 198 cases reported from Pakistan; 196 WPV1 and two WPV3. In **Afghanistan**, wild poliovirus transmission was lower in 2010, compared with 2009 but it increased during the year, 2011 [113]. It reported 80 cases, all of wild poliovirus type 1 [98]. During year 2011, the polio destruction efforts in Africa have had intermingled effects. 350 cases of wild poliovirus were calculated from 12 **AFR countries**, recording a decline by 47% (i.e. from the 657 cases reported in 2010). WPV cases in Angola decreased from 33 in 2010 to just 5 in 2011, DRC reported 93 cases compared to 100 cases in 2010 while In Chad, the number of cases also decreased to 26 from 132 cases in 2010. **Nigeria,** a polio-endemic AFR country, showed an increase in wild poliovirus cases in 2011 to 62 polio cases (47 of the total cases were WPV type 1 and 15 cases were WPV type 3) compared to 21 cases in 2010 [99]. In 2011, there were nine countries affected by a total of 11 WPV outbreaks, reporting 79 cases [98]. China was one of these nine affected countries reporting a first outbreak of 21 WPV 1 in the WHO **Western Pacific Region** since 1997 [98]. In this year, there was an outbreak of

cVDVP type 2 in Nigeria, reporting 34 cases, 11 cases were also reported in DR Congo, 9 in Somalia, 9 in Yemen and one case each in Niger and in Afghanistan [110].

Towards the end of year 2011- 23 years later since the Global Polio Eradication Initiative (GPEI) was initiated, the transmission of wild poliovirus (WPV had been hindered in all countries with the exception of Nigeria, Pakistan and Afghanistan [99].

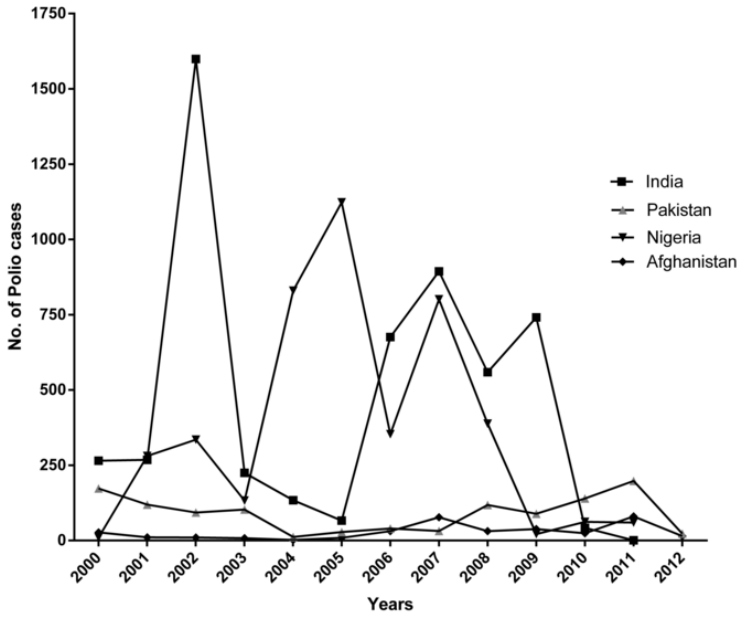
Year 2012

In January 2012, the Executive Board of the World Health Organization (WHO) announced global polio eradication as a "programmatic emergency for global public health" [114].

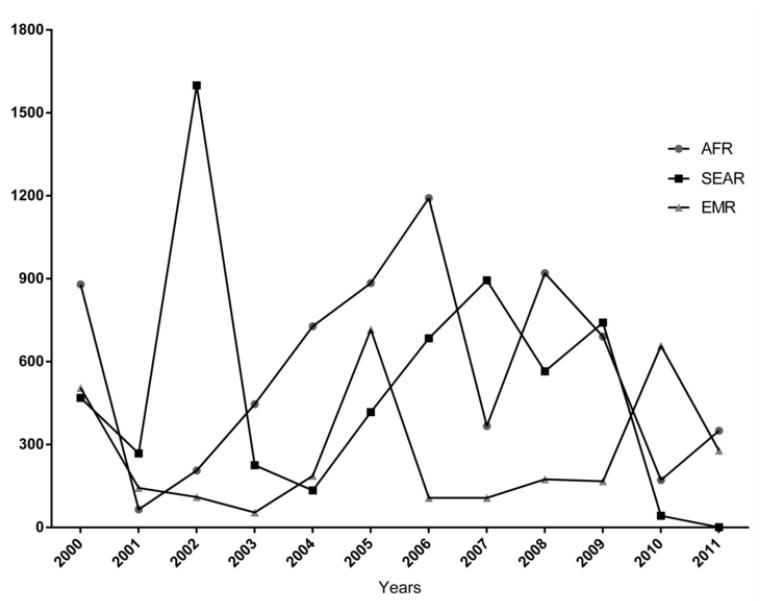
Only three countries of the world (Pakistan, Afghanistan and Nigeria) remain polio-infected, compared to more than 125 infected countries in 1988- the smallest polio-infected geographic area in history [43].

From January-March 2012, there were 6 cases of wild poliovirus type 1 reported from **Afghanistan**, 28 polio cases (21 WPV1 and seven WPV3) were identified from **Nigeria**, and 15 cases were identified from Pakistan, from which 13 were WPV1, one WPV3, and one mixed WPV1/WPV3. There is no case yet reported from India since the last case in January 2011. Thus, In January 2012 India recorded one year without any polio case paving the way for regional certification of the south-east region (SEAR) in February 2012 [98]. There were few countries who re-established polio transmission as a result of importations: Angola and DR Congo reported no polio case during January to March 2012 while Chad identified 2 wild poliovirus type 2 cases. In year 2010 and 2011, many countries were affected by the outbreaks of poliomyelitis but there is no case, as yet, reported in 2012 in any country worldwide.

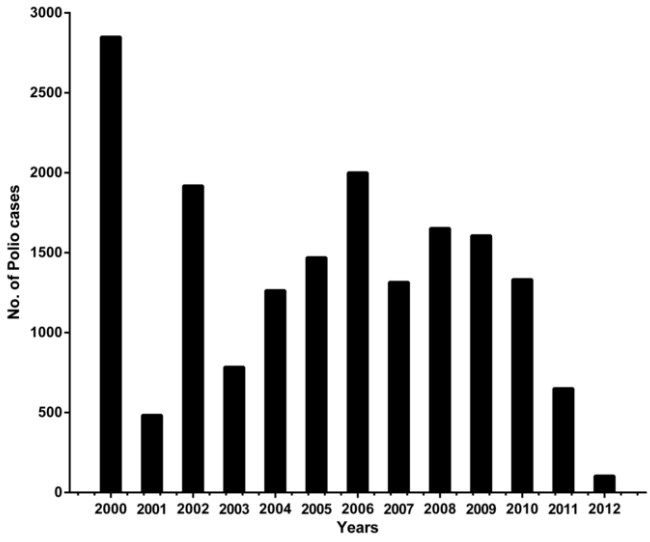
In year 2012, 1 cases of cVDVP type 2 was reported in Nigeria and 14 cases in DR Congo [98]. A summary of incidence of polio over decade (2000-2012) in epidemic countries, different regions of world and throughout the world is shown in graph 1, 2 and 3.



Graph 1. The incidence of polio cases in the epidemic countries is shown. The x-axis shows number of years while the y-axis shows number of polio cases reported



Graph 2. EMR (Eastern Mediterranean Region), AFR (African Region) and SEAR (South-East Asia Region) report polio cases in the period of 2000-2012



Graph 3. The number of polio cases reported globally (x-axis) are plotted against the 12 years (2000-2012). The graph line shows average of reported cases

Year 2013

The main reservoir area in Pakistan is in North Waziristan, Federally Administered Areas (FATA). During the past four months (August to December, 2013), 52 cases of wild poliovirus have been reported, with evidence of potential threat of widespread geographic transmission across the country. New wild type polio cases are being re-infected due to neighboring Afghanistan and in Middle East countries.

In Afghanistan, all wild type polio cases are linked to cross border transmission with Pakistan. In Nigeria, over the past four (September to December, 2013) months only four cases have occurred which are geographically restricted areas primarily to Kanod and Borno states. But within Africa, like Bandadir and Somalia, no cases of wild type poliovirus have been reported since July 2013 (Table 1, 2) [115].

Table 1. Wild Poliovirus (WPV) cases [115]

Total cases	Year-to-date 2013	Year-to-date 2012	Total in 2012
Globally	362	215	223
In endemic countries	138	210	217
In non-endemic countries	224	5	6

Table 2. Case Breakdown by country [115]

Countries	Year-to-date 2013				Year-to-date 2012				Total in 2012	Date of most recent case
	WPV1	WPV3	W1W3	Total	WPV1	WPV3	W1W3	Total		
Pakistan	77			77	54	2	1	57	58	1-Dec-13
Afghanistan	11			11	35			35	37	12-Nov-13
Nigeria	50			50	99	19		118	122	8 -Oct-13
Chad					5			5	5	14-Jun-12
Cameroon	4			4				0	0	30-Oct-13
Somalia	183			183				0	0	9-Oct-13
Syrian Arab Republic	17			17				0	0	8-Oct-13
Ethiopia	6			6				0	0	19-Sep-13
Kenya	14			14				0	0	14-Jul-13
Niger								0	1	15-Nov-12
Total	**362**	**0**	**0**	**362**	**193**	**21**	**1**	**215**	**223**	
Total in endemic countries	**138**	**0**	**0**	**138**	**188**	**21**	**1**	**210**	**217**	
Total outbreak	**224**	**0**	**0**	**224**	**5**	**0**	**0**	**5**	**6**	

2. CHALLENGES IN PAKISTAN FOR ACHIEVING POLIO- FREE STATUS

The lack of awareness against polio is one of the major factors hampering the efficiency of polio campaigns. Moreover, the polio campaigns have also been halted in the tribal regions like Waziristan, which are currently under military tensions. People of Waziristan are boycotting the polio vaccine campaigns in attempt to protest against the armed force stay and US drown attacks. But by doing so, they are risking the health of around more than 350,000 children who will remain vulnerable to polio at all times [116].

The over-dosage of polio vaccine is a usual practice in Pakistan and thus another major challenge towards polio eradication from the country. Children born during the time period ranging from 1994 to 2003 are thought to have received 30 times greater dose than the prescribed one [117]. As there is no recent research done yet to evaluate and validate the side-effects due to over-dosage of polio vaccine, it is considered to be safe by most of the doctors but the scientist have several concerns regarding its safety as it might be a potential source of circulating vaccine derived polio viruses (cVDPV).

3. CONCLUSION

As long as a single child remains infected with poliomyelitis, all other children worldwide are at risk of getting polio-infected. Thus, the remaining three polio-endemic countries remains a great threat to the all the countries worldwide. The 2010-12 strategic plan by GPEI sets out an aggressive programme that aims to eradicate poliomyelitis from the remainder countries by the year 2013. According to present reports, India has a good chance of restricting poliovirus transmission by the finish of year 2012 while Pakistan and Nigeria remains a major concern. We recommend that achieving access in FATA be top priority for Pakistan's polio program and all who support it, using all diplomatic means available. Our view remains that complete global eradication of poliomyelitis will require great efforts in prioritizing polio efforts in the global political sphere and strengthening routine immunizations in many of the polio- affected countries, and across the world. This remains a great challenge but the fail now would lead to widespread deaths and sufferings throughout the world.

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