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Adverse Post-Vaccination Events (APEs) in Mali Hospital Following Astrazeneca COVID-19 Vaccine Immunization in Mali

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Abstract **Original Research Article**

The health crisis caused by the coronavirus disease that emerged in late 2019 has not spared Mali, where it was identified as of March 25, 2020. In order to reduce the burden of the disease, preventing severe cases and deaths through the reduction of the virus circulation, Mali is considering, as a first step, the access to the COVID-19 vaccine to vulnerable people, in particular the socio-health personnel. The first vaccine used in our country was Astrazeneca, which, like all drugs, has side effects. Objectives: To identify adverse post-vaccine events (APEs) following Astrazeneca vaccination against COVID-19 and to establish their management. Methodology: This was a descriptive, cross-sectional study with retrospective data collection that took place from March 31, 2021 to October 24, 2021 including the two rounds of covid_19 vaccinations with Astrazeneca at the Mali Hospital level, the first round of which was launched from March 31, 2021 in Mali. It included all vaccinees with an adverse or unexpected sign, abnormal laboratory result, symptom, or illness following vaccination, whether or not causally related to the use of the vaccine. ***Results:*** During the 2 vaccination campaigns, we collected 20 cases of IPD out of a total of 312 recorded at the national level, i.e. a prevalence of 6.41%. The 56-65 age group was more represented in 5 cases (25%) with an average age of 42. Female sex was dominant with a sex ratio of 0.82, cases from commune VI were more reported, 7 cases (35%), the majority of the ILI appeared within 48 hours after vaccination, 15 cases (75%), hypertension was the most frequent medical history, 8 cases (40%). The most noted risk factor for coagulation was sedentary lifestyle, 9 cases (69.23%), heat at the injection site was the most frequent local reaction, 5 cases (38.46%), general aches and pains in the muscles were the most frequent systemic manifestations, 19 cases (13.48%). 11%), high fibrinogen levels 1 case (10%), high factors VIII and IX each 2 cases (22.22%), hospitalization concerned 13 cases (65%), we observed 17 cases (85%) of minor PADI and 3 cases (15%) of severe PADI, paracetamol was the most prescribed molecule in 18 cases (14.75%), the evolution during the treatment was favorable in 17 cases (85%), 3 complications (15%). ***Conclusion:*** This study allowed us to identify, classify and manage cases of AEFI related to Astrazeneca vaccination in a multidisciplinary context.

Keywords: Adverse Events Post Immunization (AEFI), Astrazeneca, Mali Hospital, Bamako, Mali.

INTRODUCTION

An emerging respiratory disease that appeared in China in late 2019 before spreading worldwide, Coronavirus disease of 2019 (COVID-19) is caused by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) [1].

As of May 3, 2021 the world has recorded a total of 152.387.917 cases of COVID-19 reported in the 223 affected countries and territories worldwide [2].

In Africa, as of May 3, 2021, a total of 4.570.906 confirmed cases have been reported, of which 122,264 deaths have been recorded, representing a case-fatality rate of 2.7% [2].

In Mali as of May 2021, 407 new cases and 33 deaths bring the total number of cases to 14,265, including 517 deaths [3].

While the SARS-COV-2 epidemic was overwhelming Europe with a new wave, the vaccine of the Anglo-Swedish laboratory Astrazeneca was the object of several criticisms, suspected of serious hematological adverse effects [4].

Like all drugs containing active ingredients, vaccines are subject to pharmacovigilance, which aims to identify the occurrence of adverse events and determine whether they are related (causal) to its administration [5].

The World Health Organization (WHO) and the European Medicines Agency (EMA) quickly stated that the benefit-risk balance remained in favor of the Astrazeneca vaccine [4, 6, 7].

At the same time, the first vaccination campaign was launched in Mali on 31 March 2021. By that time, the country had received 396,000 doses of Astrazeneca vaccine under the Covax initiative.

To our knowledge there have been few data on adverse events related to Astrazeneca vaccine immunization in Mali. The objective of this study is to evaluate and manage adverse events reported in hospitals in Mali during the weeks of vaccination with this molecule.

METHODOLOGY

This was a descriptive and cross-sectional study with prospective data collection that took place after the two rounds of vaccination against covid_19 with Astrazeneca at the Mali Hospital.

Inclusion Criteria :Any person vaccinated with Astrazeneca with an adverse or unexpected sign, abnormal laboratory finding, symptom, or illness following vaccination, whether or not causally related to the use of the vaccine, during the period from day 1 of the campaign to 42 days after the end of the campaign in the MAPI management unit of the Mali hospital.

Any patient presenting spontaneously during curative consultations for symptoms that appeared after vaccination and that he/she links to this vaccination.

Any patient in whom the health worker thinks that the patient has PID and who has also been notified in a hospital or non-hospital setting.

Exclusion Criteria : Any person vaccinated with Astrazeneca with adverse events before day 1 of the campaign or after day 42 of the end of the campaign.

Any Astrazeneca-related PAD not identified in the Mali hospital departments.

Any patient, in whom the health worker judges that the adverse events are not related to Astrazeneca vaccination.

Data were entered using a pre-designed survey form on Word 2019 software and/or analyzed with SPSS version 26.0.

RESULTS

During the 2 vaccination campaigns, we collected 20 cases of IPD out of a total of 312 recorded at the national level, i.e. a prevalence of 6.41% of IPD in Mali. The most represented age group was 56-65 years, 5 cases, i.e. 25% (Cf table 1) with an average age of 42. The female sex was dominant, 9 men against 11 women (see table 2) with a sex ratio of 0.82. Retired people were the most represented professional group, 4 cases (20%), and cases from the commune VI were more reported, 7 cases (35%). The majority of adverse events occurred within 48 hours after vaccination, 15 cases (75%) (see table 3), hypertension was the most frequent medical history, 8 cases (40%) (see table 4). The most noted risk factor for coagulation was a sedentary lifestyle, 9 cases (69.23%) (Cf table 5). Heat at the injection site was the most frequent local reaction, 5 cases (38.46%) (see Table 6). General aches and pains were the most frequent systemic manifestations, 19 cases (13.48%) each (see Table 7). During the complementary examinations, we noted coagulation factor disorders: elevated fibrinogen levels in 1 case (10%), elevated factor VIII and factor IX in 2 cases each (22.22%) (Cf table 8). Hospitalization concerned 13 cases (65%), we observed 17 cases (85%) of minor PAD and 3 cases (15%) of severe PAD (Cf table 9), paracetamol was the most prescribed molecule, 18 cases (14.75%) (Cf table 10). The evolution during the treatment was favorable in 17 cases (85%), 3 complications (15%).

Table 1: Distribution of cases by age

Age range (year)	Workforce	percentages
15-25	4	20
26-35	2	10
36-45	2	10
46-55	2	10
56-65	5	25
66-75	4	20
76-85	1	5
Total	20	100

Table 2: Distribution of cases by gender

Sex	Workforce	percentages
Female	11	55.0
Male	9	45.0
Total	20	100,0

Table 3: Breakdown by time to onset of AEFI

Time to onset (hour)	Workforce	Percentages
1 - 48	15	75.0
49 - 97	3	15
> 97	2	10
Total	20	100,0

Table 4: Breakdown by medical history

Medical background	Workforce	Percentages
High Blood Pressure	8	40
Asthma	5	25
Diabetes	2	10
Atopic Land	2	10
Asthme + Venous Insufficiency + Renal Insufficiency	1	5
heart disease	1	5
COPD	1	5
Total	20	100

Table 5: Distribution of cases according to coagulation risk factors

Coagulation risk factors	Workforce	Percentages
Sedentary lifestyle	9	69.23
Obesity	1	7.69
Viral infection	1	7.69
Toxic Consumption	1	7.69
contraceptive	1	7.69
Postoperative	0	0
Postpartum	0	0
Bacterial Infection	0	0
Sepsis	0	0
Trauma	0	0
Prolonged bed rest	0	0
Autoimmunity	0	0
Total	13	100

Table 6: Distribution of cases according to the local reaction of the injection site

Local reaction	Workforce	Percentages
Heat	5	38.46
Redness	3	23.07
Pain	2	15.38
Urticaria Pruritic Rash	2	15.38
Swelling	1	7.69
Total	13	100

Table 7: Distribution of cases according to systemic reaction

Systemic reaction	Workforce	Percentages
General stiffness	19	13.48
Muscle aches	19	13.48
Fever	17	12.05
Headaches	16	11.34
Loss of appetite	15	10.63
Dizziness	13	9.21
Faintness	9	6.38
Chills	8	5.67
Insomnia	7	4.96
Respiratory distress	5	3.54
Nausea	4	2.83
Vomiting	2	1.41
Diarrhea	2	1.41
Drowsiness	2	1.41
Anaphylactic shock	2	1.41
Consciousness Disorder	1	0.70
Total	141	100

Table 8: Breakdown of cases according to paraclinical examinations

Paraclinical examinations	Normal		Anomaly		Total
	Workforce	percentages	Workforce	Percentages	
blood sugar	16	88.89	2	11.11	18
PT (Prothrombin count)	16	100	-	-	16
creatinine	15	88.23	2	11.76	17
TCA (Active Partial Pain Time)	15	100	-	-	15
GE (Drops and thick)	15	93.75	1	6.25	16
RDTs (Rapid Diagnostic Tests)	14	70	6	30	20
CRP (C-Reactive Protein)	12	70.59	5	29.41	17
NFS (Complete Blood Count)	11	57.89	8	42.11	19
Grouping/Rhesus	10	100	-	-	10
Fibrinogen	9	90	1	10	10
Serum electrolytes	9	100	-	-	9
Factor VIII	7	77.78	2	22.22	9
Factor IX	7	77.78	2	22.22	9
Troponin	7	100	-	-	7
D-dimers	7	100	-	-	7
CPK-MB (Creatine Phosphokinase MB)	6	100	-	-	6
Triglyceride	5	100	-	-	5
Total cholesterol	5	83.33	1	16.67	6
Thoracic CT Angio	4	36.36	7	63.64	11
LDLc (low-density lipoproteins)	4	80	1	20	5
HDLc (high-density lipoprotein)	4	80	1	20	5
ECG(Electrocardiogram)	4	80	1	20	5
Brain Scan Angio	3	75	1	25	4
CPK MB	3	100	-	-	3
Ultrasound Doppler Lower Limbs	3	100	-	-	3
HbsAg (Hbs Antigen)	2	100	-	-	2
HCV (Hepatitis C serology)	2	100	-	-	2
HIV	2	100	-	-	2
Chest X-ray	2	66.67	1	33.33	3
Echocardiography	2	66.67	1	33.33	3
Spine scan	2	66.67	1	33.33	3
IgE (immunoglobulin E)	1	33.33	2	66.67	3
X-ray of the face skull	1	50	1	50	2
EMG (Electromyogram)	-	-	1	100	1

Table 9: Distribution of cases by type of APEs

APEs		Workforce	Percentages	Total
Minor	Covid_19 reactivation	6	85	17
	General signs of AEFI	11		
Serious	Acute pulmonary embolism + venous thrombosis of MI	1	15	3
	Cerebral Thrombosis	1		
	Guillain Barre syndrome in spinal cord disease	1		
Total		20	100	20

Table 10: Breakdown of cases by treatment

Processing	Workforce	Percentages
Paracetamol	18	14.75
Serum Salty	16	13.11
Serum Glucose	14	11.48
Enoxaparin	13	10.66
Antibiotic	10	8.20
Methylprednisolone	9	7.38
Ringer lactate	6	4.92
Azithromycin	6	4.92
Chloroquine	6	4.92
Vitamin C	6	4.92
Morphine	3	2.46
Adrenaline	3	2.46
ORS	2	1.64
Nefopam	2	1.64
Chlorpheniramine	1	0.82
Acenocoumarol	1	0.82
Metoclopramide	1	0.82
Omeprazole	1	0.82
Nebulization	1	0.82
Rivaroxaban 15mg	1	0.82
Spironolactone 75mg	1	0.82
Losartan + HCT 50/12.5	1	0.82
Total	122	100

DISCUSSION

During the 2 vaccination campaigns, we collected 20 cases of PADI out of a total of 312 recorded at the national level, i.e., a prevalence of 6.41% of PADI in Mali linked to Astrazeneca. According to the latest update published on April 2 (based on data up to March 25) by the Agence nationale de sécurité du médicament et des produits de santé (ANSM) in France, Astrazeneca's vaccine is estimated to have caused 7,439 cases of adverse events out of nearly 2.5 million injections, i.e., 0.3%[8], while in Canada the prevalence was 0.06% for the entire Covid-19 immunization [9].

The age group 56-65 years was more represented 5 cases (25%) with an average age of 42.3 years. According to ANSM [10] reactogenicity was generally milder in intensity and reported less frequently in older adults (≥ 65 years).

Female gender was dominant with a sex ratio of 0.82. According to the Amiens CRPV report #10 [11], the same finding was made with a sex ratio of 0.038. This disproportion is not related to a marked imbalance in the number of women vaccinated, but it could reflect a greater reactogenicity in women, as mentioned in previous studies with influenza vaccines [12].

Cases from commune VI were more notified 7 cases (35%). This high representation of cases from this area can be explained by the geographical position of the hospital in Mali which is located in this commune. In Ontario, in their weekly surveillance report [9] this was reported: The geographical distribution of the number of reports of IPD is based on the health territory of residence of the case when the IPD occurred, it does not reflect the location of the vaccine administration.

The majority of PFDs occurred within 48 hours of vaccination (75%). According to the ANSM [10] Astrazeneca-related cases of flu-like symptoms with a time of onset <24 h were observed. Hypertension was the most frequent medical history 8 cases (40%). Hypertensive attacks occurred in patients with MAPI for whom a history of hypertension was found in 34% or in whom risk factors for hypertension were found [11]. The most noted clotting risk factor was sedentary lifestyle 9 cases (69.23%), however in relation to

clotting risk factors, the European Medicines Agency (EMA) mentioned that "for the moment, reviews have not identified specific risk factors for these very rare events such as age, gender or a medical history including blood clot problems" [13]. Heat at the injection site was the most frequent local reaction, 5 cases (38.46%), general soreness and muscle pain were the most frequent systemic manifestations 19 cases (13.48%) each. These local and systemic reactions were found in an ANSM publication [10].

	Frequency of identified adverse events (%)	
Type of adverse reaction identified	ANSM [10]	Our Study
Local reaction: injection site reaction (tenderness, pain, heat, pruritus, bruising at injection site)	≥ 10	3 - 39
Systemic reactions: headache, nausea, myalgia, arthralgia, fatigue, malaise, fever, chills		
Local reaction: injection site reaction (swelling, erythema)	1 - 10	2 - 23
Systemic reaction: vomiting, diarrhea, fever		
Lymphadenopathy, Decreased appetite, Dizziness	0.1 - 10	0 - 11
Drowsiness	0.1 - 1	1.41

During the complementary examinations, we found abnormalities such as thrombocytopenia in 8 cases (42.11%). This thrombocytopenia was commented on in the report of the CRPV of Amiens [11], which had found 15 cases (5.75%). In Germany, the trigger for the suspension of the Astrazeneca vaccine was an opinion of the Paul Ehrlich Federal Institute for Vaccines and Biomedicine [14] and the report of an unusual number of cerebral venous sinus thrombosis associated with platelet deficiency (thrombocytopenia) and hemorrhage. This association was found in seven cases (as of March 15, 2021, the date of the suspension in Germany), and a chronological association compatible with vaccination with the Astrazeneca COVID-19 vaccine was pointed out [14]. Hospitalization concerned 13 cases (65%), which was observed in 5% of cases in the report of the CRPV of Amiens [11].

Paracetamol was the most prescribed molecule in 18 cases (14.75%), which is justified by the predominance of side effects such as general aches and pains, muscular pain, and fever, which were treated with paracetamol. The prescription of this molecule was mentioned by the ANSM [10], which stipulates that "in case of fever and/or pain, we recommend the use of paracetamol at the lowest dose and for the shortest time possible".

The evolution during treatment was favorable in 17 cases (85%), 3 complications (15%) and 0 deaths. Among these complications, the formation of blood clots in the form of venous thrombosis was observed in 2 cases, one of which was cerebral and the other pulmonary in the form of venous thrombosis of the lower limbs. These events have affected a total of 12 people in France since the beginning of the vaccination, 4 of whom have died. At the European level, according to the European Medicines Agency (EMA), these serious adverse events have involved 258 serious cases, with 45 deaths [8].

The other complication was Guillain-Barré syndrome. This syndrome was noted in 8 cases in the report of the CRPV of Amiens [11]. During the course of our study, no case of death was reported in a hospital in Mali, but during the same period a case of severe IPD with death in Commune 6 of Bamako during a consultation at the Sorila medical practice was reported [15].

Limitations of the study

Descriptive and cross-sectional study with retrospective collection of data based on information provided in the MAPI files (medical records, hospitalization registers), which were often incompletely filled out, sometimes requiring telephone calls from patients.

The high cost of complementary examinations, which were paid for by the hospital in Mali, was more or less assured. The limited sampling and the short duration of the study.

The non-use of the chi-square statistical test to compare our results with other studies.

CONCLUSION

There is no such thing as a "perfect" vaccine that protects all those who receive it and is completely free of adverse effects. Therefore, we recommend that anyone who experiences persistent adverse events such as dizziness, headache, visual disturbances, nausea/vomiting, shortness of breath, severe pain in the chest, abdomen, or extremities, or who develops skin bruising (petechiae) beyond the vaccination site should seek prompt medical attention. Healthcare professionals should be alert to signs and symptoms suggestive of thromboembolism in individuals vaccinated with

Astrazeneca's vaccine in order to perform appropriate biological and imaging tests for early management of these individuals.

Conflict of Interest: None

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