IMAGE: A MAP OF THE STARS OF THE ORION CONSTELLATION

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ABSTRACT

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Herpes simplex virus still represents the most common and potentially serious viral complication in pregnant women. This cross -sectional hospital-based study aimed to estimate the seroprevalence of infection among pregnant women attending Martyr Ali Abd Alfattah Hospital, eighty blood specimens were collected from pregnant (aged between15 and 45years old) that were suspected to be infected, with herpes simplex viruses from Khartoum during November 2019. Specimen examined by using immunochromatography test (ICT) For IgM antibodies. One full drop of serum and two drops of buffer in the specimen was added to the well of the test device and then start the timer, the result was read after 15 minutes. The result showed that all eighty specimens were negative for herpes simplex virus infection. This indicates low prevalence of herpes simplex virus infection among pregnant women attending Martyr Ali Abdelfattah Hospital. Additional studies are needed to sure the low prevalence of the HSV and educational programs must be applied to present the risk factors, route of transmission and method of prevention.

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I. INTRODUCTION

Herpes simplex virus type 2(HSV2) one of (TORCH), that can cause illness in pregnant women and are responsible for spectrum of diseases ranging from gingivostomitis to keratoconjunctivitis, encephalitis, genital diseases and infection of newborn, these entire infectious agents induce a shift of immune response during pregnancy from Th2 to Th1 and apoptosis which can be observed clinically as abortion process [1].

HSV2 is the second most prevalent sexually transmitted viral infection worldwide and the most common cause of genital ulceration in the developed world [2]. Intra-uterine herpes simplex virus infection can cause significant morbidity and mortality in the developing fetus if the pregnant mother gets acute infection during pregnancy, the acquisition of genital herpes during pregnancy result in spontaneous abortion, stillbirth, intrauterine growth retardation, preterm labor, congenital and neonatal herpes infections. Genital herpes varies between different countries and between groups of individuals depending on the demographic and clinical characteristics [3].

HSV2 is neurotropic virus that has a large linear, double-stranded DNA genome protected by a capsid with icosahedral symmetry surrounded by an envelope consisting of a lipid bilayer with embedded glycol proteins, having yet a protein acetous region between the capsid and envelope called tegument, belong to alpha herpesvirinae subfamily, within the family Herpesviridae [4]. Transmitted across mucosal membranes and

non-intact skin that migrate to nerve tissues where they persist in a latent state [5]. The danger of intrauterine HSV transmission is highest during the first 20 weeks of gestation this because a Newly infected mother does not have antibodies against the viruses which can lead to congenital anomalies, stillbirth, or abortion [6,2]. Pregnancy induces a transient immunosuppression which increases the vulnerability of pregnant women to viral infections. In addition, may lead to fetal death. After an incubation period of about a week, the active phase begins during the active phase, the virus multiplies explosively between 50,000 and 200,000 new visions are produced from each infected cell [7].

The primary symptomatic genital herpes infection is usually the most severe, especially in women, it causes blistering and ulceration of the external genitalia and cervix leading to vulvar pain, dysuria, vaginal discharge and local lymphadenopathy [8].

II. MATERIAL AND METHOD

This study was Survey Study. Study to detect Herpes Simplex Virus infection among pregnant women Attending Martyr Ali Abdel Fattah Hospital in Khartoum state Sudan between the periods from September to December2019. This study was done on pregnant women attending Martyr Ali Abdlfattah hospital. A total of 80 blood samples were collected from pregnant women, all blood sample were transferred into plain blood containers then centrifuged at 3000 RPM for 3 min to obtain sera.

2.1 Immunochromatography test (ICT)

The TORCH Combo Rapid test cassette (serum plasma) is a qualitative lateral flow immunoassay for the detection of IgM antibodies to rubella, CMV, Toxo in serum or plasma specimen, in this test antigen of Rubella, CMV, Toxo and HSV are coated in the test line regions of each section in the test. During testing, the serum or plasma specimen reacts with mouse anti human IgM coated particles in the test strip. The mixture then migrates upward on the membrane by capillary action and reacts with the Rubella, CMV, Toxo, and HSV specific antigens on the membrane in the test line regions of the respective sections. The presence of a colored line in the test line region or particular section indicates a positive result for the corresponding infection while its absence indicates a negative result for the infection. To serve as procedural control a colored line will always appear in the respective control line regions of all the four strips indicating that proper volume of specimen has been added and membrane wicking has occurred.

All sera were tested according to the procedures described by the cassette. One free fall drop of the serum was added into test wells and 2 drops of buffer then it was incubated for 10 minutes. One colored line appears in the control line region and non-appearance of a visible line in the test line region indicates HSV negative result.

III. DATA ANALYSIS

Data were analyzed by computer system using statistical package for social science (spss).

Ethical Consideration

Permission from hospital was applied and verbal consent was taken from participants and was only be used for research purposes.

IV. RESULTS

Overall prevalence of HSV-2 IgM antibodies in pregnant women attending Mayer Ali Abdallfattah Hospital was 0% and all 80 women serum samples studied were showed a negative result (Table1).

The statistical analysis showed that 58(72.5%) of this study group were pregnant women less than 30 years age and the rest 22 (27.5%) were aged more than 30 years old (Table 2). The result also demonstrates that only 9 (11.25%) of this study group have a history of abortion. However, 71 (88.75%) participants have no history of miscarriage (Table 3). Additionally, 28 (35%) of our study population were in first trimester of pregnancy at time of study while 25 (31.25%) and 27 (33.75%) of this study group were in second and third trimester respectively. The result of blood group frequencies for the pregnant women

those participated in our study was revealed that O+ve was the most popular blood group with percentage of 37.5% followed by A+ve, AB+ve, B+ve, O-ve, A-ve, with percentage of 30%, 11.25%, 10%, 5% and 3.75% respectively. However, the least blood group detected in pregnant women were AB-ve and B-ve with percentage of 1.25% for both (Table 5). Only 16% of pregnant women in this study have a vaginal discharge in their clinical history (Figure 1).

Table 1: Result of HSV-2 ICT test among pregnant women

Elements	Positive	Negative	Total	Percent
Anᵢ-HSV IgM	0	80	80	0%

Table 2: Distribution of the study population according to age group

Elements	Frequency	Percent
Less than 30	58	72.5%
More than 30	22	27.5%
Total	80	100.0%

Table 3: Distribution of the study population according to history of abortion

Elements	Frequency	Percent
Abortion	9	11.25%
No abortion	71	88.75%
Total	80	100.0%

Table 4: Distribution of the study population according to trimester

Elements	Frequency	Percent
First	28	35%
Second	25	31.25%
Third	27	33.75%
Total	80	100.0%

Table 5: Distribution of the study population according to blood group

Elements	Frequency	Percent
O+ve	30	37.5%
O-ve	4	5%
AB+ve	9	11.25%
AB-ve	1	1.25%
A+ve	24	30%
A-ve	3	3.75%
B+ve	8	10%
B-ve	1	1.25%
Total	80	100.0%

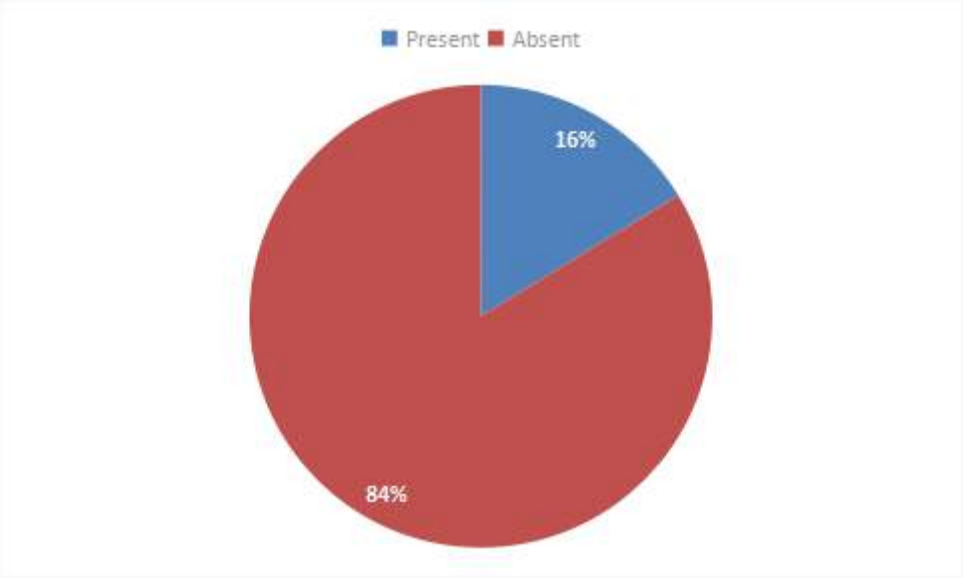

Figure 1: Distribution of the study population according to present of vaginal discharge

V. DISCUSSION

Herpes simplex virus is one of TORCH infections group (Toxoplasma gondii, Rubella, Cytomegalovirus, Herpes simplex). It is a worldwide obstetrical problem, where transplacental transmission of the infection may result in serious congenital diseases the importance of this study is due to the importance of herpes simplex viruses because they are responsible for a spectrum of diseases ranging from gingivostomatitis to keratoconjunctivitis encephalitis, genital diseases and, it is known to be one of the causes of spontaneous abortion.

The result of ICT for IgM was negative for all eighty studied women, this indicate to low prevalence of HSV-2 among pregnant women at Martyr Ali Abdelfattah Hospital, but we cannot confirm the absence of HSV-2 by this study due to small sample size which need confirmatory study with inclusion of large study population. Our study agreed with that of El-Amin *et al.,* 2013 in Sudan which done in National Ribat teaching hospital they examined three hundred and fifty-six women delivered during the period of the study for HSV-2 IgM and IgG and they found that forty-five women (34.6%) tested positive for the IgG of herpes viruses but no one of them test positive for IgM test by ELISA (9). However, our study was disagreed with that of Hadeel *et al.,* 2015 in Sudan whom found that the prevalence of HSV-2 IgM antibodies among 90 pregnant women was 2 (2%) (10). Also, our result was disagreed with Alaa *et al* study in Sudan in 2018 whom demonstrate that the prevalence of HSV-2 IgM antibodies among 90 pregnant women was 7 (7.7%) of which only 6 were confirmed by molecular study (11). In addition, our result was also disagreed with Indian study conducted by Biswas *et al* in 2011 which conducted in five northeastern states to understand the epidemiology and role of risk factor associated with HSV seroprevalence with an aim focused toward prevention and they found that overall HSV seroprevalence was 8.7% (142/1640). The disagreement between our result and other findings may be due to usage of more advance technology with more sensitivity rate like ELISA and PCR in other test compared to ICT in our study. In addition, lacking of funding lead us to include only small sample size, on the other hand we find some other studies include more sample size.

VI. CONCLUSION

All the pregnant women in this study are negative for HSV IgM by ICT, most women are on intermediate level of education and most women were at first trimester. Some symptoms of HSV are found on some of pregnant women but there no positive result.

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Enhancement of Aglaonema Commutatum Propagation using Thidiazuron and Naphthalene Acetic Acid in Vitro

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ABSTRACT

Chinese evergreen (Aglaonema commutatum) is being cultivated recently as a decorative plant in Egypt. In the present study trials were done to micropropagate it in vitro. For this purpose nodal segments were excised from shoots and cultured on Murashige and Skoog's (MS) culture media augmented with naphthalene acetic acid (NAA) 0.1 and 0.5 mg/l in combination with thiadiozhuros (TDZ) O.5 , 1.0 and 2 mg/l, followed by transfer to hormone –free culture media added to it active coal, for four weeks and regularly subcultured four successive times . Results of the present study have shown that 0.5 mg/l NAA + 2 mg/l TDZ for eight weeks were superior to the other hormonal combinations used. This treatment led to significant increases over the other treatments in number of shoots obtained per explant, the number of leaves per shoot and number of roots per plantlets 4.67±0.58, 2±0.00, 7.00±1.00 respectively, the average length of shoot and roots 8.50±0.10, 7.33±0.15 cm respectively, and the average fresh weight per regenerant 9.99±0.22 gram with a corresponding dry weight 0.30±0.01 gram. The obtained regenerates were easily acclimatized and transferred to pots.

Keywords: chinese evergreen, decorative plant, nodal segments, tissue culture.

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The obtained results may facilitate production of A. cammutatum on the commercial level in our country.

Keywords: chinese evergreen, decorative plant, nodal segments, tissue culture.

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I. INTRODUCTION

Aglaonema commutatum is a monocotyledonous plant belonging to family Araceae, known as aroids, it is an ornamental plant important in interior landscaping due to its attractive brightly colored leaves. Vegetative methods are the traditionally propagation means for Aroid plants, such as division or cuttings (Chen and Stamps, 2006). Vegetative propagation is associated with diseases spread between plants (Norman and Yuen, 1998). Tissue culture techniques, are known to be faster than traditional methods of propagation and many reach commercial production levels within 2–3 years (Henny and Chen, 2003).

Compared to other plant growth regulators (PGRs), TDZ is a more powerful and potent synthetic growth regulator exhibiting both auxin and cytokinin (CK)-like effects on plants. Despite this unique and dual effect, TDZ's action is often overgeneralized and referred to as a cytokinin. It is therefore important to note that although TDZ can mimic the effects of auxins and CKs. Structurally it differs from both of these PGR groups, possessing both phenyl and thiadiazole functional groups. Both groups are required for biological activity (Mok et al, 1987). TDZ can be used for regeneration at lower concentrations making it a valuable commercial agrochemical (Guo et al, 2011).

The aim of the present study is to micropropagate Aglaonema commutatum in vitro using NAA And TDZ.

II. MATERIAL AND METHODS

Mother cultures of *Aglaonema commutatum* were obtained from tissue culture lab, EL-Zohria Botanical Garden, Cairo, Egypt. The experiment was carried out in Plant Tissue Culture Lab of Agric. Botany Dept., Fac. of Agric. Ain Shams Univ., during the years of 2019–2020.

Explants: Nodal segments of three month old sterile plantlets.

Culture media: Murashige and Skoogs basal medium (1962) containing sucrose 30 g/l and solidified with Agar 7 gram/l. pH adjusted to 5.7 prior autoclaving, the medium was divided into glass jars (200 ml) containing 40 ml of the testing medium. The culture medium was autoclaved at 121°C and 1.1Kg cm^{-2} for 20 min.

Growth regulators: Naphthalene acetic acid (NAA) and Thidiazuron (TDZ).

Table 1: Various concentrations of Growth regulators used

Treatments	Growth regulators (mg/l)	
	NAA	TDZ
1	0	0
2	0.1	0.5
3	0.5	1.0
4	0.5	2.0

Culture conditions : Cultures were incubated in a growth room 25 ± 2°C under illumination intensity of 1500 lux day light located 40 cm above the top of cultures (40 watts white fluorescent lamp). The photoperiod was 16 hours light and 8 hours dark that is automatically controlled.

Statistical analyses: Data represent mean ± standard deviation of 3 different values. The experiment was arranged in a complete randomized design (Gomez and Gomez, 1984) with ten replicates (jars), each replicate has four explants. The obtained results were subjected to statistical analysis of variance (ANOVA) in statistics (8^{th} edition analytical software, USA) by (Steel *et al*, 1997). Differences between means were contracted by LSD meth.

II. RESULTS AND DISCUSSION

Ornamental plants are an important element of indoor decorating and coordination. *Aglaonema commutatum* is a beautiful indoor plant, distinguished by the beauty of its pied leaves, but there are great difficulties in propagating it by traditionally methods. Traditionally methods of vegetative propagation of plant have many disadvantages such as infection with bacterial and fungal diseases as stated by (Ranjan Kumar Tarai et al, 2020). It has been mentioned by_(Ajit Kumar Sahoo. *et al*, 2019) that growth and development of plants is controlled by two sets of internal factors, such as nutrition and hormonal constituents.

In this experiment, plant growth regulators were used *in vitro* with success and positive results were achieved in multiplication and production of a lot of plants during a short period as indicated in figure (1) and table (2). In addition it was observed that there is a direct relationship between cytokinin concentration and the percentage of segments that gave shoots, such results were observed by (Ahmed *et al*, 2008).

Table 2 : Effect of different growth regulators treatments on % of bud multiplication of *Aglaonema commutatum in vitro*

Treatments	growth regulators		% of bud multiplication
	NAA (mg/l)	TDZ (mg/l)	
Treat. 1	0.0	0.0	0.0
Treat. 2	0.1	0.5	67
Treat. 3	0.5	0.1	73
Treat. 4	0.5	2.0	88

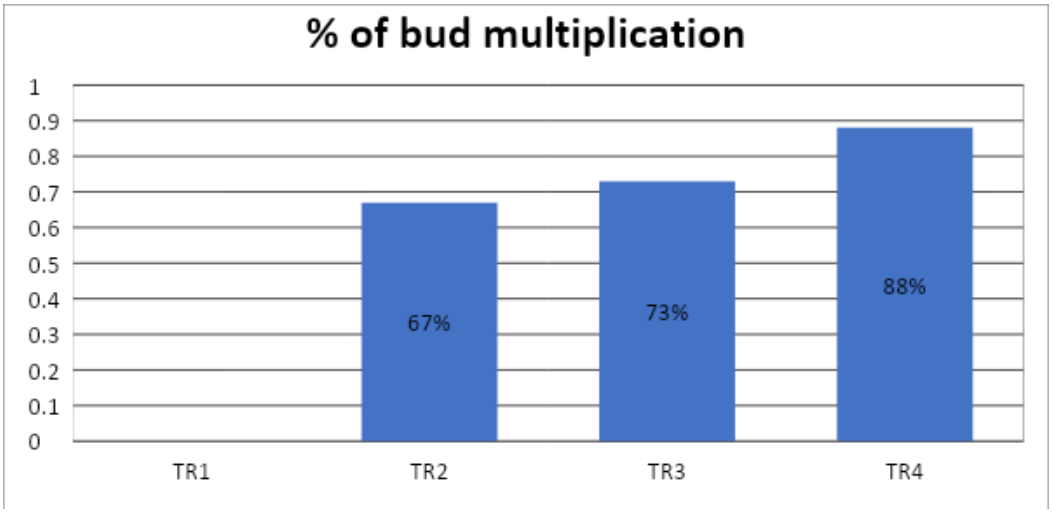

Figure 1: Effect of different growth regulators treatments on % of bud multiplication of *Aglaonema commutatum in vitro*

Table 3: Effect of different growth regulators treatments on different morphogenic parameters of *A. commutator in vitro*

Treatments		Growth parameters						
NAA (mg l^{-1})	TDZ (mg l^{-1})	No of shoots/ explant	No of leaves/ shoot	Shoot length (cm)	Root length (cm)	No of roots/ plantlet	F.W shoot system	D.W shoot system
0.0	0.0	0.00 ^{d}	0.00 ^{c}	0.00 ^{d}	0.00 ^{d}	0.00 ^{c}	0.00 ^{d}	0.00 ^{c}
0.1	0.5	1.00±00 ^{c}	1.00±00 ^{b}	3.50±0.10 ^{c}	3.03±0.21 ^{c}	4.33±0.58 ^{b}	2.26± 0.06 ^{c}	0.05±00 ^{c}
0.5	1.0	2.00±00 ^{b}	1.00±00 ^{b}	5.77±0.06 ^{b}	5.03±0.15 ^{b}	5.33±0.58 ^{b}	4.57± 0.05^{b}	0.12±0.01 ^{b}
0.5	2.0	4.67±0.58 ^{a}	2.00±00 ^{a}	8.50±0.10 ^{a}	7.33±0.15 ^{a}	7.00±1.00 ^{a}	9.99± 0.22 ^{a}	0.30±0.01 ^{a}
LSD		0.54	0.00	0.14	0.62	1.21	0.22	0.055
Means followed by different letters are significantly different.								

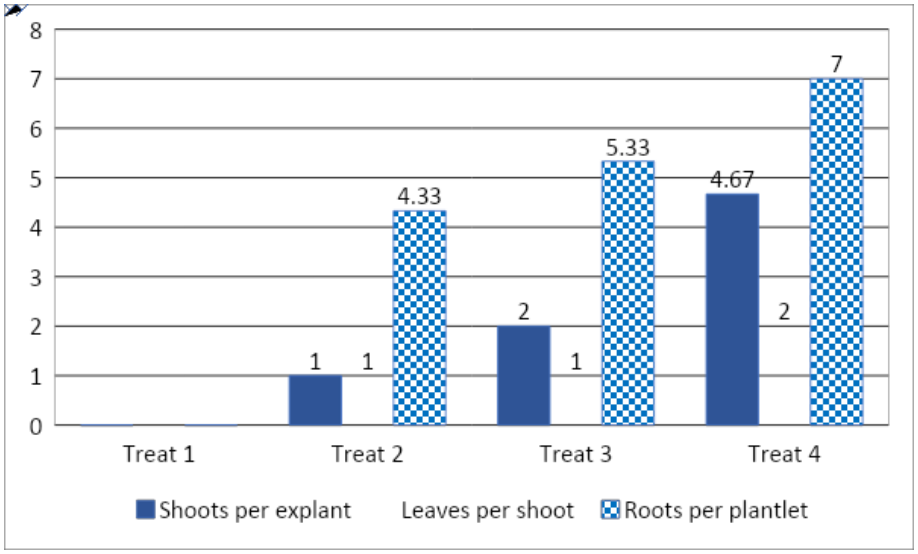

Figure 2: Effect of growth regulators treatments on number of shoots per explant and number of leaves and roots per plantlet

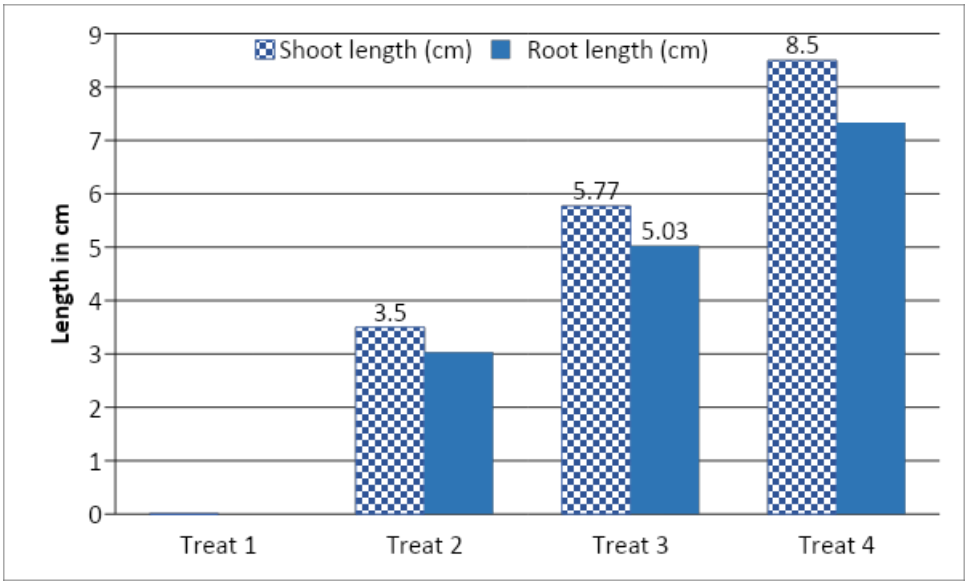

Figure 3: Effect of different growth regulators treatments on shoot and root lengths

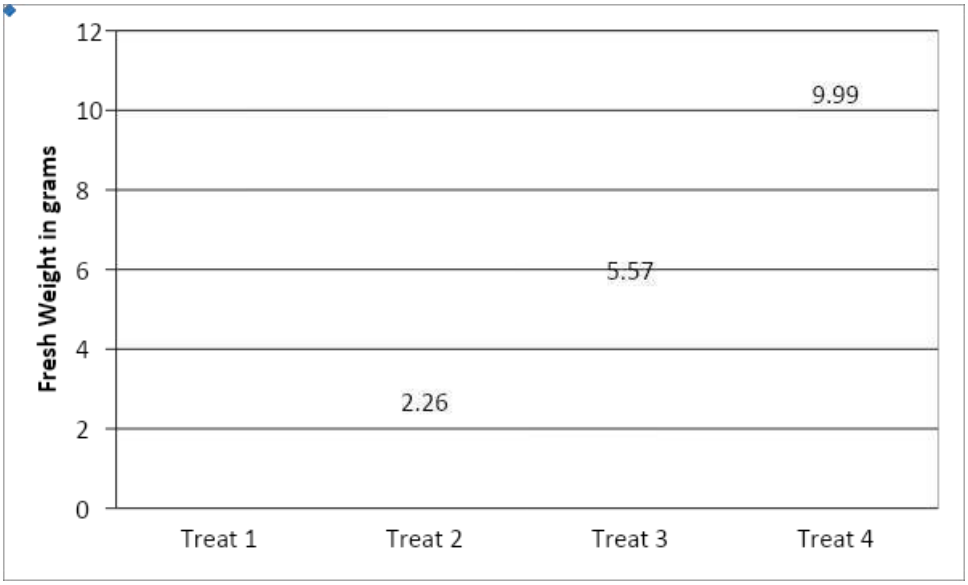

Figure 4: Effect of different growth regulators treatments on the fresh weight of shoot system

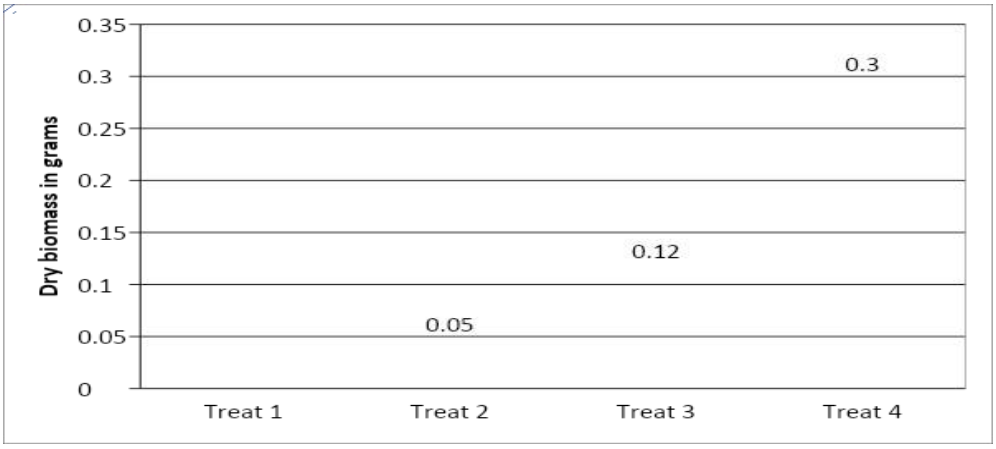

Figure 5: Effect of different growth regulators treatments on the shoot dry biomass

Data clarified in table (2) and figure (1) showed the effect of various NAA & TDZ concentrations on the shoot induction percentage. The data revealed that TDZ treatments promoted and significantly increased all growth parameters.

In table (3) fig (2), (3), (4) and (5).The highest and significant number of shoots obtained per explant, leaves per shoot and roots per plantlets 4.67±0.58, 2±0.00, 7.00±1.00 respectively, the average length of shoot and roots 8.50±0.10, 7.33±0.15 cm respectively, and the average fresh and dry weight per plantlets 9.99±0.22, 0.30±0.01gram respectively were recorded with 0.5 mg/l NAA+ 2 mg/l TDZ.

In many studies e.g. (Asma *et al*, 2020) indicated that both auxins and cytokin is were necessary for maximum response *in vitro*, but in other studies like (Mariani *et a,* 2011) reported that TDZ is CK-like compounds that can promote shoot proliferation and had important role for induction of shoots, and play role of both auxins and cytokin is. Direct shoot organogenesis, can be limited by the availability of preexisting meristems on the explants and a low multiplication rate. Also, (Fang *et al,* 2013) reported that when the cytokinin were used alone, it failed to induce adventitious shoots, while in contrast using of an auxin with a cytokinin may often prove useful.

Diverse factors may affect the capability of TDZ to induce shoot bud initiation and growth including: concentration of TDZ, cultivar, type and source of explant, age or phase of growth, presence of other PGRs, balance of endogenous growth regulators and presence of light (Sanikhani *et al,* 2006; Visser *et al,* 1992).

(Mariani *et a,* 2011) demonstrated that using 1.50 mg/l TDZ on *Aglaonema sp*. micropropagation was successful. This suggests that a low concentration of TDZ (0.15 mg/l) favors the tissue culture of Araceae plants. In the same trend (Fang *et al,* 2013) excised the single stem nodal segments from the elongated shoots for Aglaonema 'Lady Valentine and treated them with different combinations of NAA and TDZ, the average of adventitious shoots per stem segment was 10.9 produced with 0.5 mg/l NAA and 2 mg/l TDZ. The number of adventitious shoots induced varied greatly from one stem segment to another. Since the adventitious shoots most likely originated from the meristematic cells located on the periphery of the axillary bud, it is suspected that the number of meristematic cells present on the nodal region of each stem segment is highly variable. The variable response of stem nodal segments may due to age, size or other conditions of the plant material, as observed in *Dieffenbachia compacta* by (Azza *et al,* 2010; Chen and Yeh 2007; Zhang *et al*, 2004 and Huetteman and Preece, 1993) who observed that low concentrations of TDZ could induce shoot multiplication while the corresponding BA concentrations could not. Superiority of TDZ for the node and shoot induction was reported in *Aglaonema* sp. and a number of other ornamental plant species (Mariani *et al*, 2011). The probable reason for this may be attributed to the ability of plant tissues to absorb and use TDZ more readily than other PGRs. Adding of 0.5 mg/l BA + 0.5 mg/l Kin to the cultures saved the plantlet from stunted growth and encouraged the continuation of the growth of new shoots to some extent. It was mentioned that by (Ahmed et al. 2008) that adding cytokinins stimulate the cell division and growth of shoot.

Root morphogenesis was done on MS medium without PGR, where plantlets rooted well. The non-prerequisite for an auxin at the rooting stage shows that the plantlets may contain enough indogenous auxin (Murti *et al,* 2012) for root initiation.

(Mariani, 2011) explained in his research that the survival rate of live plants after the seedlings acclimatization stage was 100%, but the seedlings were transferred on sphagnum moss then after that transfer to soil, while in figure (6 –f,g,h,i) clearly the success of the seedling acclimatization phase, directly without gradations in pots containing regular loam soil is illustrated.

More or less similar results were carried out by (Kaviani *et al,* 2019) on *Aglaonema widuri* and

(El-Mahrouk, 2016) on *Aglaonema nalantine* where the authors could successfully enhance micropropagatio using NAA and TDZ which were used in the present study.

Figure 6:

a) Mother plant
b) Separated micro-shoots
c) Nodal segments
d) Shoot & root morphogenious in jars
e) Shoot & root morphogenious
f) Acclimatized plantlets 1 month old
g) Acclimatized plants 3 months old
h) Acclimatized plants 5 months old
i) Acclimatized plants 7 months old

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Factors Determining Early Antenatal Care Utilization in Uganda

Ruth Atuhaire, Will Kaberuka, Leonard.K. Atuhaire & R.Wamala

ABSTRACT

Antenatal care utilization is a success story in Uganda (at least 90% of expectant mothers received ANC); however, accessing the first antenatal within the first three months of pregnancy is vital, a period for essential interventions like identification and management of obstetric complications. This study aimed at establishing factors contributing to early antenatal care service utilization in Uganda.

We used a sample of 10,152 women of reproductive ages (15-49), who had given birth in the five years preceding the Uganda Demographic and Health Survey. Andersen's Behavioral Model of Health Services Utilization guided the selection of covariates in the model. In contrast, binary logistic model used to analyze the relationship between early antenatal care on age, highest maternal education level, marital status, wealth quintile, distance to a health facility, cost of service, availability of health worker in the community, exposure to media, nature of pregnancy and parity.

Keywords: antenatal care, likelihood, timely accessibility, education completion.

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Antenatal care utilization is a success story in Uganda (at least 90% of expectant mothers received ANC); however, accessing the first antenatal within the first three months of pregnancy is vital, a period for essential interventions like identification and management of obstetric complications. This study aimed at establishing factors contributing to early antenatal care service utilization in Uganda.

We used a sample of 10,152 women of reproductive ages (15-49), who had given birth in the five years preceding the Uganda Demographic and Health Survey. Andersen's Behavioral Model of Health Services Utilization guided the selection of covariates in the model. In contrast, binary logistic model was used to analyze the relationship between early antenatal care on age, highest maternal education level, marital status, wealth quintile, distance to a health facility, cost of service, availability of health worker in the community, exposure to media, nature of pregnancy and parity.

Predictors that had relatively increased odds of early antenatal care utilization include mothers who are age 19-35, completed primary seven, distance is not a problem, readily available community health workers, and no complicated pregnancy. Furthermore, mothers aged 15-18, did not complete secondary level, not married, travel a long distance to a health facility, with the cost of service being problematic and parity were associated with reduced odds of early antenatal care utilization.

The study recommends that government should promote female education to primary seven completion hence delaying child marriages, reduce on costs of utilizing antenatal care by enacting the insurance bill and encouraging pregnancy centering and sensitizing the public on benefits of early utilization leading to improved maternal and newborn outcome during pregnancy.

Keywords: antenatal care, likelihood, timely accessibility, education completion.

I. INTRODUCTION

Maternal health care comprises dimensions of antenatal/prenatal, childbirth delivery/intranasal, postnatal and neonatal care to reduce maternal morbidity and mortality (Rice, 2019; UBOS, 2017; UNICEF, 2019). Utilization includes ensuring comprehensive antenatal care (ANC) coverage for all pregnant women, the first ANC within the first three months of pregnancy (Rutaremwa, Wandera, Jhamba, Akiror, & Kiconco, 2015; Srivastava, Mahmood, Mishra, & Shrotriya, 2014; Wang & Hong, 2015). WHO (2015) defines antenatal care (ANC) as monthly visits during the first two trimesters (from week 1–28), fortnight visits from 28th week to 36th week of pregnancy and weekly visits after 36th week until delivery (delivery at week 38–42) at a health facility. Early ANC implies the utilization of antenatal care and services within the first trimester (Mamba, Muula, & Stones, 2017; Say et al., 2014; Tunçalp, Souza, & Gülmezoglu, 2013).

Even though the government has prioritized measures for improvement of maternal health services, most women access antenatal services late (Finlayson & Downe, 2013; Kawungezi et al., 2015; Kisuule et al., 2013; Mamba et al., 2017). According to UDHS 2016 survey, the median

gestational age when women make their first antenatal visit is approximately 4.7 months. Though studies have focused on the utilization of antenatal care leading to a success story in Uganda (Kawungezi et al., 2015; Mugarura, Kaberuka, Atuhaire, Atuhaire, & Abaho, 2017; Wiluna et al., 2015), hardly any information is available on the causes of early antenatal care utilization.

We carried out the study to establish factors contributing to early antenatal care service in Uganda. Andersen's Behavioral Model of Health Services Utilization guided the selection of covariates in the model. The exogenous variables selected as determinants of early antenatal care services that are predisposing and enabling factors included mother's wealth quintile, marital status, parity, maternal age at last birth, maternal highest education level, exposure to mass media, distance to a health facility, cost of service, if either the pregnancy was wanted or not, and if the pregnancy was complicated or not.

The study utilized data obtained from the 2016 Uganda Demographic Household and Health Survey (UDHS). The survey was a follow up to the previous UDHS carried out in 1988/89, 1995, 2000/2001, 2006, and 2011 and is implemented by the Uganda Bureau of Statistics. For all the years, the woman's questionnaire collected information from all eligible women aged 15-49 years (those aged 15-49 minus those who had no live birth in the five years preceding the survey). Respondents were asked questions about their demographic and household characteristics, maternal and child health indicators. Table 1 shows the measurements of the variables adopted for the study.

Table 1: Measurement of variables used in the study

Code	Variable	Description	Coding if any	Data type
Y_1	Early Antenatal	Timing of the first antenatal visit	1. Accessed antenatal care within first trimester. 2. Accessed after first trimester	Binary
X_1	Age of the women	Age of the woman at the time of the survey	1. 15-18 2. 19-35 3. 36-49	ordinal
X_2	Parity	Children ever born by the woman		Count
X_3	Highest maternal education level	Mother's highest level of education	1. some primary 2. completed primary seven 3. some secondary 4. completed secondary six	ordinal
X_4	Income	Wealth quintile of the household	1. Poor 2. middle 3. Rich	ordinal
X_5	Marital status	Marital status of the woman	1. Unmarried 2. Married	nominal
X_6	Pregnancy wanted	If the mother wanted the last pregnancy	1. Yes 2. No	nominal
X_7	Exposure to mass media	Women who listen to radio, read newspapers or watch television	1. Exposure 2. Non exposure	nominal
X_8	Pregnancy complications	If the pregnancy was complicated or not	1. Yes 2. No	nominal
X_9	Community factors	Availability of community health worker	1. Yes 2. No	nominal
X_{10}	Distance to the health facility	If the distance from home to the health facility is a problem or not.	1. Big problem 2. not big problem	nominal
X_{11}	Direct costs/fees	If cost paid while accessing a service is a problem or not	1. big problem 2. not	nominal

Data were analyzed using STATA 13.0. We performed a descriptive summary of the variables in the study in the form of frequency tables (see table2). At the bivariate level, we ran differentials in antenatal care with each predictor using a binary logistic regression model to estimate the odd ratios unadjusted (see table 3). This stage helped us determine the significant variables which we used in the final analysis. Variables that had a relatively small probability value of 0.05 or less were considered for inclusion in the final analysis to ascertain the predictors of early antenatal care utilization. At multivariate level, significant exogenous factors were included in the logit model, which allows each category of an unordered response variable compared to an arbitrary reference category.

The following equation expresses the relationship between early antenatal care and its predictors.

$$\ln\left(\frac{\Pr(Y_1=1)}{1-\Pr(Y_1=1)}\right) = \beta_0 + \hat{\beta}_i \hat{X}_i + U_i$$

Where; Y_1 represent the early ANC, β_o represent the intercept of the model, β_i is the matrix of the slope coefficients and x_i is the matrix of independent variables (maternal education, marital status, age at last birth, parity, complications or not, whether the pregnancy was wanted or not, exposure to mass media, readily available community health workers, cost of services offered, and distance to a health facility), and, u_i is the error term.

The outcome variable considered in this study was early antenatal care and the predictors were; maternal age at birth, maternal education, parity, wealth quintile, marital status, costs incurred at health facility and distance to health facility. Community factors were availability of a worker and health facility in an area, while predisposing and need factors were exposure to media, pregnancy complications and if pregnancy wanted or not. Table 2 presents the frequencies of these study variables.

Table 2: Frequency distribution table of the study variables

Variable	Frequency	Percent (%)
Early Antenatal care		
Went within the first trimester	2897	28.5
Went after the first trimester	7255	71.5
Age		
15-18	2347	23.1
19-34	5154	50.8
35-49	2651	26.1
Highest Maternal education level		
Some Primary	4406	43.4
Completed primary seven	1827	18.0
Some secondary	3198	31.5
Com leted secondar six	721	7.1
Marital status		
Married	3189	31.4
Unmarried	6963	68.6
Wealth quintile		
Poor	4128	40.7

Middle	1912	18.8
Rich	4112	40.5
Distance to health facility		
Big problem	3957	38.9
Not big problem	6195	61.1
Cost of service		
Big problem	4763	46.9
Not big problem	5389	53.1
Availability of a health worker in community		
Readily available	7258	71.5
Not readily available	2894	28.5
Exposure to media		
Exposed to media	8110	79.9
Not exposed to media	2042	20.1
Pregnancy wanted		
Yes	6185	60.9
No	3967	39.1
Complications		
Yes	660	6.5
No	9492	93.5

Results show that less than 3 out of 10 women accessed their first ANC within 3 months of pregnancy. Significant delays for first ANC visit have been observed in other countries including Rwanda where only 38% of women have an ANC visit in their first three months of pregnancy (Manzi et al., 2014) and Ethiopia where more than half of women had a delayed ANC (Wiluna et al., 2015; Yesuf & Calderon-Margalit, 2013).

Women have shown not to access early ANC checkup, an essential time recommended for receiving medical information over maternal physiological and biological changes in pregnancy and prenatal nutrition, health personnel checking the mother's medical history, for example if a mother had a history of an ectopic pregnancy to avoid reoccurrence, test for HIV status, birth defects and blood pressure (Carroli, Rooney, & Villar, 2005; Chama-Chiliba & Koch, 2013; Chukwuma, Wosu, Mbachu, & Weze, 2017; Ebonwu, Mumbauer, Uys, Wainberg, & Medina-Marino, 2018; Mamba et al., 2017).

Half of the sampled women were of age 19-35, the most fertile period (Elster, 1984). More than 5 out of 10 women had completed primary seven (56.6%) though very few women had completed (56.6%) though very few women had completed secondary six (7.1%). A good proportion of women were unmarried (68.59%). Women from a poor background were almost equal to those from the rich background (40.66% and 40.51% respectively), and women from an average background were the fewest (18.83%). Six in every ten women (61.02%) didn't point out distance to health facility as a big problem. There was a slight difference between women who thought cost of service was a big problem compared to those who thought it was not (46.92% and 53.08% respectively). Most health workers were readily available in the community (71.5%), and most women were exposed to at least one form of media (79.89%). Results in Table 2 further indicated that at least 6 in every 10 women wanted the pregnancy and a small proportion of women had complicated pregnancy (6.5%). On average, women had 3 children ever born with a standard deviation of 3 children.

Table 3: Differentials in Early ANC utilization

Factor	Unadjusted OR(95% CI)	Adjusted OR(95% CI)
Age ì5-18 19-34 35-49	1.890(1.756-1.99)* 0.980(0.881-1.023) 1.200(0.990-1.245)*	1.0 0.92(0.82-1.00) 1.18(1.08-1.26)*
Highest Maternal education level Some primary Completed primary seven Some secondary Completed secondary six	1.321(1.001-1.456) 1.687(1.482-1.812)* 0.790(0.633-0.985)* 1.126(0.833-1.511)	1.0 1.68(1.58-1.81)* 0.9(0.63-0.98) 1.12(0.83-1.51)
Marital status Unmarried Married	0.845(0.750-0.987)* 0.990(0.856-1.099)*	1.0 0.93(0.89-1.20)*
Wealth quintile Poor Middle Rich	0.932(0.876-1.007) 0.857(0.716-1.027) 0.863(0.734-1.011)	- - -
Distance to health facility Not Big problem Big problem	1.512(1.234-1.650)* 0.974(0.859-1.103)*	1.0 0.97(0.85-1.10)*
Cost of service Not big problem Big problem	1.031(0.987-1.143)* 0.605(0.472-0.822)*	1.0 0.50(0.37-0.82)*
Availability of a health worker in community Not readily available Readily available	1.021(0.954-1.170)* 1.061(0.970-1.182)*	1.0 1.06(0.97-1.18)*
Exposure to media Exposure Non-exposure	0.923(0.876-1.100) 1.077(0.927-1.251)	- -
Pregnancy wanted No Yes	0.823(0.765-0.987)* 1.170(1.033-1.367)*	1.0 1.15(1.03-1.36)*
Complications No Yes	0.621(0.543-0.876)* 1.942(1.733-2.367)*	1.0 2.04(1.89-2.26)*
Parity	0.942(0.918-0.967)*	0.89(0.81-0.92)*

*Note 1: (OR): Exponential coefficients; CI: confidence intervals; * indicates variables with p<0.05 Note 2: estimates based on weighted data*

Table 3 indicates that the factors associated with relatively increased odds of early ANC were women with age of 19-34 years, completing primary seven, distance to health not being a big problem, cost of service not being a big problem, a readily available health worker in a community compared to when a health worker is not readily available, women's desire for pregnancy and complications ($p<0.05$).

The factors that were associated with relatively reduced odds of early ANC were women aged 15-18 years, not completing secondary, being married compared to unmarried, distance to a health facility as big problem, cost of service being a big problem, women who didn't want the pregnancy, without complications, and parity ($p<0.05$).

Additionally, the factors that significantly contributed to early ANC were: maternal age, maternal education, marital status, distance to health facility, cost of attaining service, availability of a health worker in the community, desire for pregnancy, complications and parity ($p<0.05$).

Holding other factors constant, adult mothers age 35-49 had an 18% increased odds of utilizing early ANC as compared to teenage mothers age 15-19 (OR=1.18). Women who completed primary seven had a 68% increased odds of utilizing ANC within the first trimester as compared to a woman who had incomplete primary education (OR=1.68). A married woman had a 7% reduced odds to utilize early ANC as compared to an unmarried woman (OR=0.93).

Women were distance to a health facility a big problem that had a 3% reduced odds to utilize early ANC as compared to women were distance to a health facility is not a big problem(OR=0.97). Women with the cost of service problems were half as likely to utilize ANC within the first trimester as compared to women with no problems (OR=0.5). Women in communities with readily available health workers had a 6% increased odds of utilizing early ANC as compared to women in communities with no readily available health workers (OR=1.06).

Women who wanted the pregnancy had a 15% increased odds of utilizing ANC services within the first trimester as compared to women who did not (OR=1.15). Women with complicated pregnancy were twice as likely to utilize early ANC compared to women with no complications (OR=2.04). One more live child ever born in a household lowered the odds on average by 11%, holding other factors constant (OR=0.89).

Results from this study are in agreement with most scholars who revealed that adult women and high education levels are associated with early utilization of antenatal care services (Ensor & Cooper, 2004; Mamba et al., 2017; Sacks et al., 2017; Wilunda et al., 2014), and in affirmation with studies in Kenya (Arunda, Emmelin, & Asamoah, 2017; Kitui, Lewis, & Davey, 2013; Magadi, Madise, & Rodrigues, 2000), Rwanda (Golooba-Mutebi, 2011; Hagey, Rulisa, & Perez-Escamilla, 2014; Manzi et al., 2014), India (Pallikadavath, Foss, & Stones, 2004; Singh, Rai, Alagarajan, & Singh, 2012; Srivastava et al., 2014), Zambia (Sacks et al., 2017) and in the USA (Yaya, Bishwajit, & Shah, 2016). However, some studies reported a strong association between teenage mothers and early use of ANC (Mosiur Rahman, Haque, & Sarwar Zahan, 2011; Ochako, Fotso, Ikamari, & Khasakhala, 2011).

Additionally, women delayed to attain early ANC services because of direct costs involved, overcrowding in hospital, staff attitude, and long distances to a health facility in Ethiopia (Abosse, Woldie, & Ololo, 2010; Wudineh, Nigusie, Gesese, Tesu, & Beyene, 2018), Rwanda (Golooba-Mutebi, 2011; Hagey et al., 2014), Benin (Dansou, Adekunle, & Arowojolu, 2017), India (Pallikadavath et al., 2004; Singh et al., 2012; Srivastava et al., 2014) and Tanzania (Mrisho et al., 2009).

A study by Finlayson and Downe (2013) reveal that barriers to early ANC utilization are driven by views that pregnancy is a healthy state, women's limited financial resources, and not getting it right the first time due to inadequate services for mother with other children.

In essence: The right timing of ANC leads to avoiding most of the maternal health conditions during pregnancy.

Pregnancy should be an enjoyable stage in every woman's life, and mothers should be mindful of the benefits of utilizing early antenatal healthcare service to reduce incidences of maternal and neonatal underlying conditions, especially abortions. Though maternal mortality was declining and increased proportionate of women attain antenatal care services, late timing will continue to pre-dispose women and newborns to the risk of morbidity and mortality.

The majority of women have not completed primary and secondary levels of education. This is because childbirth in Uganda starts as early as 13 years (UBOS, 2017) when the girls are supposed to be at school. To improve the utilization of early ANC, there is a need to formulate policies and design maternal health service programs that sensitize women about the benefits of comprehensive ANC visits. Mothers should be encouraged to give "first visit within three months of pregnancy" priority and avoid delayed access for better maternal and neonatal outcomes.

The government of Uganda and other stakeholders should reduce the costs of attaining health services by enacting the bill on insurance, encourage pregnancy centering, and strengthen the position of community health workers.

There is need for female child education completion, scholarship programs and legislation against early marriages promotions for young women to remain in school longer. Educated women are better positioned to acquire, understand, and utilize knowledge when exposed to media on maternal health information.

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Assessment of Transcranial Duplex Abnormalities in Children with Sickle Cell Disease

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ABSTRACT

Background: Children with sickle cell disease (SCD) who showed abnormal transcranial duplex (TCD)abnormal velocities can be managed by regular blood transfusion for prevention of stroke.

Aim of this work: To assess abnormal TCD velocities in pediatric patients with SCD with their relation to stroke and other complications using multimodal approach through clinical, neuroimaging and neurophysiological studies.

Study design: cross-sectional study. Place and Duration of Study: Sample: Department of Pediatric (Hematology Unit) and Department of Neurology, Tanta University Hospital Egypt, between April 2016 and April 2018.

Methodology: This study was conducted on 50 children with SCD and 25 healthy children matched age and sex. All subjects were subjected to full history taking, neurological examination using pediatric neurological sheet, neuroimaging including: CT and /or MRI, MRA and/or CT angiography, also MRV, transcranial duplex, EEG and Stanford-Binet Intelligence scales-Fifth Edition.

Keywords: SCD, TCD abnormalities, prevention.

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ABSTRACT

Background: Children with sickle cell disease (SCD) who showed abnormal transcranial duplex(TCD)abnormal velocities can be managed by regular blood transfusion for prevention of stroke.

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Results: SCD patients showed many abnormalities on neurological examination and on different modalities of MR imaging on the brain with positive relation with many risk factors. Prophylactic blood transfusion in SCD patients with abnormal TCD had a role in reducing the incidence of stroke.

Conclusion: There was variation in neurological presentation, examination and brain imaging in cases with SCD. There was positive relation between regular blood transfusion in SCD patients and decreased risk for ischemic stroke and abnormal TCD velocity in these patients.

Keywords: SCD, TCD abnormalities, prevention.

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I. INTRODUCTION

Sickle cell disease (SCD) is an autosomal recessive hemoglobin disorder. It is a qualitative hemoglobinopathy resulting from a structural change in the sequence of amino acids on the beta globin chain of the hemoglobin molecule due to a point mutation. It is characterized by hemoglobin polymerization, erythrocyte stiffening, and subsequent vaso - occlusion (1, 2).

The most predominant form of hemoglobinopathy worldwide is sickle cell disease. It is estimated that 75-85% of children born with SCD are born in Africa (3, 4). It is common among people of Equatorial African where the prevalence ranges from 10 to 40% of the population, Saudi Arabian and Mediterranean ancestry, and now it's widespread in America and Europe (5, 6). The prevalence of SCD is 0.3% in Egypt, where the carrier rate varies from 9 to 22% (7).

In the deoxygenated condition, the hemoglobin tetramer polarizes and the cell shape becomes distorted, resulting in rigid red blood cells. Cell damage leads to hemolytic anemia and to occlusion of vessels in multiple organs, including the brain (8).

Children with sickle cell disease, present with a wide variety of neurological syndromes, including ischemic and hemorrhagic stroke, transient ischemic attacks, soft neurological signs, seizures, headache, coma, visual loss, altered mental status, cognitive difficulties, and covert or 'silent' infarction (9).

Although the prevalence of seizures in children with sickle cell disease is about10 times that of the general population, there are few prospectively collected data on its pathogenesis (10). Seizures occur in 12 to 14% of patients with sickle cell disease (SCD), herald stroke in 10 to 33%, and are associated with silent infarction (10.11).

Several Studies of cerebral blood flow (CBF) with 133 Xenon inhalation have shown that encephalopathic patients with SCD having seizures show regional hypoperfusion which may resolve at follow-up (12).

Magnetic resonance imaging (MRI) and transcranial Doppler (TCD) flow studies are useful in detecting subclinical cerebral infarction (13). The ability to predict strokes by detecting arterial stenosis with TCD and the role of chronic transfusion in prophylaxis from such strokes has led to the recommendation that TCD can be used for routine screening and that transfusion can be instituted on detection of arterial stenosis (14).

II. PATIENTS AND METHODS

This study was carried out between April 2016 and April 2018 on 50 children diagnosed by hemoglobin electrophoresis as sickle cell disease admitted at hematological unit and underwent follow up at outpatient clinic of Hematology Unit, Pediatric Department. They were aged from 2 to 18 years old including 27 males and 23 females.

There was also a control group of 25 healthy children matched with the age (3 to 16 years old) and gender including 16 males and 9 females who attended general outpatient clinic of Pediatric Department for a comparative study. Informed consent was taken from the guardian of all children and the study was approved from Faculty of Medicine, Tanta University ethical committee.

Inclusion criteria: Children suffered from sickle cell disease who developed various neurological disorders or were at risk for developing such disorders e.g. low hemoglobin, high white cell count, increased baseline of reticulocytes, previous transient ischemic event, hypertension and history of chest crisis.

Exclusion criteria: Children with other hemoglobinopathies diagnosed by hemoglobin electrophoresis.

- Children with sickle cell disease having an inborn error of metabolism already diagnosed in conjunction or screening of suspected cases of serum pyruvate, lactate or homocysteine in serum or urine to be excluded.
- Children suffering from neurological disorders especially stroke who already diagnosed as coagulopathy or vasculopathy other than sickle cell disease.

All children were subjected to: Full medical history taking, thorough neurological examination using pediatric neurological sheet, and Stanford-Binet Intelligence scales-Fifth Edition as an evaluation tool for intellectual functioning. Laboratory investigations included: complete blood picture count with differential, reticulocyte count, and renal & hepatic function tests.

Neuroimaging studies included: CT and /or MRI of the brain. Also, MRA and /or CT angiography of cerebral blood vessels when needed in some patients and transcranial color coded duplex(TCCD)(using timed average mean of maximum velocity parameter(TAMMV)). Besides, MRV when needed in some patients. Electrophysiological studies included: EEG.

Statistical analysis

The collected data were organized, tabulated and statistically analyzed using SPSS software statistical computer package V17. For quantitative data, the range, mean and standard deviation were calculated. For qualitative data, comparison between two groups and more was done using Chi-square test ($\chi 2$). Significance was adopted at $p < 0.05$ for interpretation of results of tests of significance (15,16).

III. RESULTS

There was statistically highly significant difference regarding transcranial duplex findings among patients compared with control group, with the largest number of patients (n= 28) (56%) matching with low velocity. Patients with high velocity only represented 8% of patients followed by those with very low velocity (4%)(Table 1) (Figure 1,2).

There was statistically highly significant difference regarding relation between regularity of blood transfusion and occurence of ischemic arterial stroke among patients. The highest percentage (66.67%) of patients at risk of stroke was in those with yearly blood transfusion followed by risk for patients(33.33%) with irregular blood transfusion(Table 2).

There was positive correlation between transcranial duplex abnormalities and risk for cognitive decline, MRI brain, EEG abnormalities and stroke with the highest predictive value for stroke risk (Beta: -0.644) (Table 3).

Table 1: Transcranial duplex findings among patients and control groups:

Variable	Groups				Chi-Square	
Transcranial duplex findings	Patients(n=50)		Control(n=25)			
	Number	%	Number	%	χ^2	P-value
Very low velocity	2	4.00	0	0.00	32.813	<0.001*
Low velocity	28	56.00	0	0.00		
Normal velocity	15	30.00	25	100.00		
Conditioned velocity	1	2.00	0	0.00		
High velocity	4	8.00	0	0.00		

-Very low: All vessels: < 20cm/sec - Low: All vessels: < 70cm/sec.-
Normal: All vessels: < 170cm/sec.-
Conditional: >170 /sec but < 200 cm/sec dICA, MCA, intracranial bifurcation.-
-Abnormal or high: > 200cm/sec MCA, intracranial bifurcation, dICA.

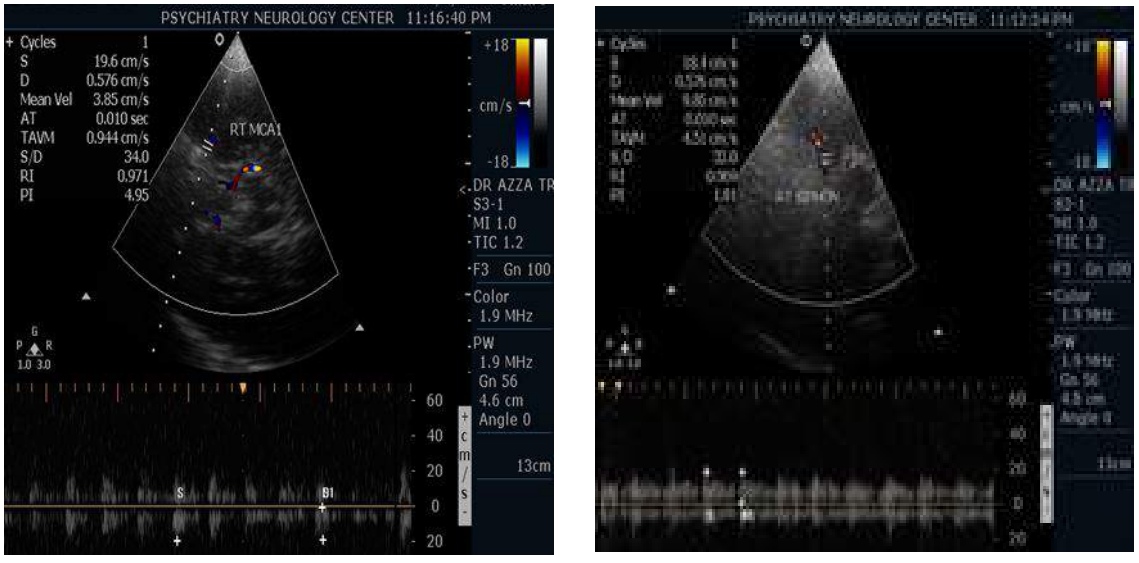

Figure 1: TCCD showing TAMV of right MCA and right siphon less than 20cm/s (very low velocity) in this case

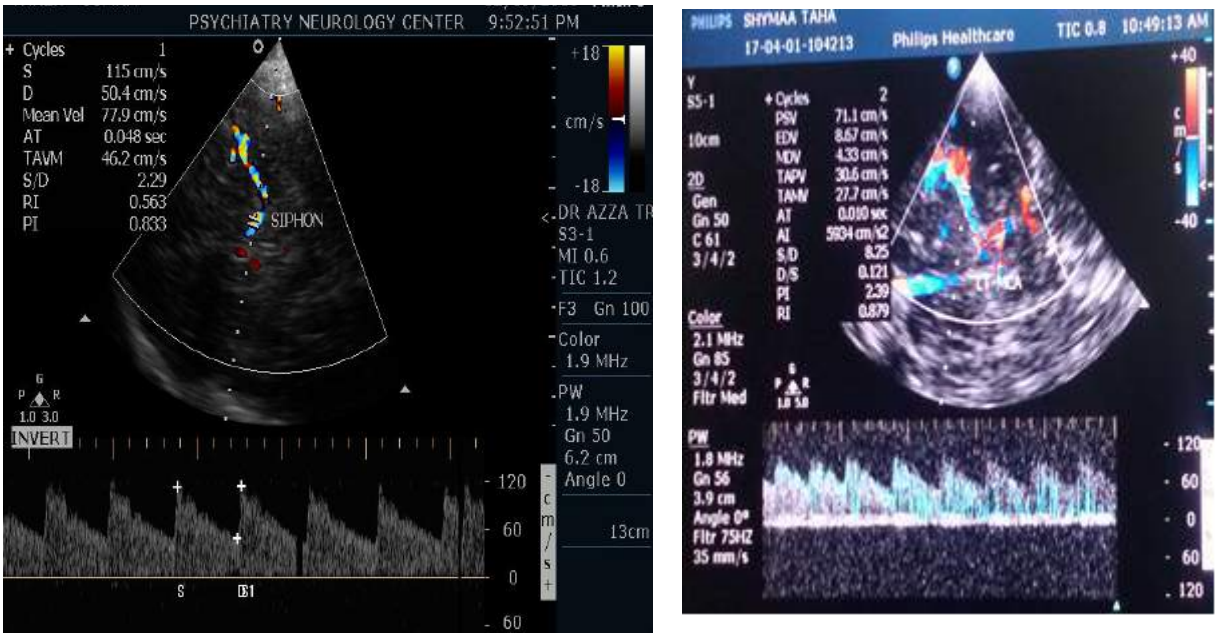

Figure 2: TCCD showing TAMV of left distal ICA (siphon)and left MCA less than 70cm/s (low velocity) in this case.

Table 2: Relation between regularity of blood transfusion and transcranial duplex findings among patients

Regular Blood transfusion	Transcranial duplex										Chi-Square	
	Very low velocity		Low velocity		Normal velocity		High velocity		Conditioned velocity			
	N	%	N	%	N	%	N	%	N	%	X^2	*P-Value*
Regular	1	50	28	100	15	100	4	100	1	100		
Every month	0	0.00	7	25.00	7	46.67	0	0.00	0	0.00	115.221	<0.001*
Every 2 months	0	0.00	11	39.29	5	33.33	0	0.00	0	0.00		
Every 3 months	0	0.00	5	17.86	2	13.33	0	0.00	0	0.00		
Every 4 months	0	0.00	2	7.14	0	0.00	0	0.00	0	0.00		
Every 5 months	0	0.00	1	3.57	0	0.00	1	25.00	0	0.00		
Every 6 months	0	0.00	0	0.00	0	0.00	2	50.00	0	0.00		
Every 7 months	0	0.00	0	0.00	0	0.00	0	0.00	1	100.00		
Yearly	1	50.00	2	7.14	1	6.67	1	25.00	0	0.00		
Irregular	1	50.00	0	0.00	0	0.00	0	0.00	0	0.00		

Table 3: Multiple regression analysis according to transcranial duplex abnormalities

	Unstandardized Coefficients		Standardized Coefficients	T	*P-Value*
	B	Std. Error	Beta		
Cognitive decline	0.137	0.229	0.088	0.600	0.552
MRI brain abnormalities	0.165	0.121	0.410	1.364	0.179
EEG abnormalities	-0.389	0.139	-0.421	-2.791	0.008*
Stroke risk	-0.702	0.345	-0.644	-2.036	0.048*
Dependent Variable: Transcranial duplex abnormalities					

IV. DISCUSSION

Transcranial duplex findings of our studied patients revealed that patients presented according to TAMM velocity by either: Very low velocity (4% of patients), low velocity (56% of patients), normal velocity (30 % of patients), conditioned velocity (8% of patients) and high (2% of patients) velocity. There was statistically highly significant difference regarding transcranial duplex findings among patients compared with control group, with the largest number of patients (56%) matched with low velocity.

This was in agreement with Zétola VF., 2012 who reported that in normal children the velocity was in the range of 90 cm/sec in the middle cerebral artery. In children with SCD the velocity was higher due to anemia and it is in the range of 130-140 cm/sec. Above 170 cm/sec, which was about 1.5 standard deviations above the mean, stroke risk increased. Over 200 cm/sec the risk of stroke rised from the baseline rate of 0.5-1%/year to the range of 10-13%/year. Values in between 170 and 200 indicated intermediate risk. Very low velocities on TCD might be found after an overt stroke. This was in agreement with Buchanan ID et al., 2013 who reported that velocities were low or absent by TCD in 10% of the SCD patients perhaps related to vasculopathies such as moyamoya or extracranial vasculopathy.

There was positive relation between regular blood transfusion in patients in this study and risk for abnormal velocity detected in transcranial duplex. The highest percentage of patients with very low velocity were those with yearly (50%) and irregular (50%) blood transfusion. The highest percentage of patients with conditioned velocity were those with blood transfusion every 7 months (100%) and the highest percentage of patients with high velocity were those with blood transfusion every 6 months (50%) followed by those with yearly blood transfusion(25%). In contrast to this, the highest percentage of patients with normal velocity were those with regular blood transfusion every month (46.67%)).

There was statistically highly significant difference between patients with regular blood transfusion and those with irregular blood transfusion as regard abnormal velocity detected on TCD. This was in agreement with Raphael JA et al., 2013 who reported that chronic blood transfusion was effective for the primary and secondary prevention of stroke as well as for reducing the risk of recurrent cerebral infarcts in children with SCD. Stroke patients were continued on monthly RBC transfusions indefinitely, with a goal HbS of less than 30%. Patients who had abnormal TCDs were also treated with monthly transfusions, with a goal HbS of 30%.

V. CONCLUSION

Most patients (56%) had low velocity according to TAMM on transcranial duplex indicating previous stroke. There was positive relation between regular blood transfusion in SCD patients and decreased risk for ischemic stroke and abnormal TCD TAMM velocity (high and very low velocity). There was positive correlation between transcranial duplex abnormalities and risk for cognitive decline, MRI brain, EEG abnormalities and stroke with the highest predictive value for stroke risk (Beta: -0.644)

5.1 Compliance With Ethical Standards

Any unexpected risks appeared during the course of the research will be cleared to the participants, their parents and the ethical committee on time.There are adequate measures to maintain the privacy of participants and confidenality of the data:

A code number to every patient with the name and address will be kept in a special file. The patient name will be hidden when using the research.The results of the study will be used only in a specific manner and not to use in any other aims. Endpoint of the research will be achieved when any of the above mentioned risks threaten the health and the quality of the life of patients.

Informed consent will be obtained from patients 18 years old or older and from the legal guardians of those younger than 18 years. Assent will be obtained from patients between 14 and 18 years old before entering the study.

Consent

All authors declare that 'written informed consent was obtained from the patient (or other approved parties) for publication of this research and accompanying images.

Ethical Approval

All authors hereby declare that all experiments have been examined and approved by the appropriate ethics committee and have therefore been performed in accordance with the ethical standards laid down in the 1964 Declaration of Helsinki.

Competing Interests

Authors have declared that no competing interests exist.

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Non-Communicable Disease Screening through Socio-Technical Lens in a Low Resource Setting

Dr Srujan Goud Janagam, Smitha Thomas Kaniyampady, Muthuraj & Dr Anupama Shetty

ABSTRACT

In the last decade, there has been an epidemiological shift from communicable to non-communicable disease and the impact of this shift is more evident in India which is witnessing rapid urbanization and lifestyle changes. NCDs are the leading causes of morbidity and mortality in India of which the 4 major NCDs (Cardiovascular Diseases, Respiratory diseases, Diabetes, and Cancer), contribute to 60% of the total deaths in the country. The key priority areas of the primary health systems in India has been the maternal health and family planning programs while the other infectious and non-infectious disease prevention had taken a back seat. Though there were structural and operational limitations in delivery of effective primary Healthcare, new age screening solutions are offering sustainable and scalable solutions with quantitative & accurate clinical decision making, referrals, data collection and disease awareness. This study examines the NCD screening solution developed by Narayana Health through the socio technical systems perspective in low resource settings.

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Non-Communicable Disease Screening through Socio-Technical Lens in a Low Resource Setting

Dr. Srujan Goud Janagam [α], Smitha Thomas Kaniyampady [σ], Muthuraj [ρ] & Dr. Anupama Shetty [Ѡ]

ABSTRACT

In the last decade, there has been an epidemiological shift from communicable to non-communicable disease and the impact of this shift is more evident in India which is witnessing rapid urbanization and lifestyle changes. NCDs are the leading causes of morbidity and mortality in India of which the 4 major NCDs (Cardiovascular Diseases, Respiratory diseases, Diabetes, and Cancer), contribute to 60% of the total deaths in the country. The key priority areas of the primary health systems in India has been the maternal health and family planning programs while the other infectious and non-infectious disease prevention had taken a back seat. Though there were structural and operational limitations in delivery of effective primary Healthcare, new age screening solutions are offering sustainable and scalable solutions with quantitative & accurate clinical decision making, referrals, data collection and disease awareness. This study examines the NCD screening solution developed by Narayana Health through the socio technical systems perspective in low resource settings.

Methods and materials: The data collected from screening solution that was developed using socio-technical system was used to assess the screening solution in addressing the gaps in NCD screening. A cross sectional study was carried out from June 2019 to January 2020 in the urban Bangalore district.

Results: A total of 16,635 individuals for screened for NCDs of whom 22.6% were hypertensives, 9.1% were diabetic, 25% were Overweight and Obese. Anaemia was prevalent in 36% of the population of which 0.4% were severe anaemics, 3.5% were moderate anaemics and 32% were mild anaemics. Of the total population screened for oral and breast cancer 98 were found to have precancerous oral lesions and 50 received confirmatory diagnosis for severe dysplasia. The innovative development of screening kit and workflow process brought in a lot of traction to the program in increasing awareness, early identification and referral to higher government health centres for confirmatory diagnosis.

Conclusion: The NCD screening solution that was developed using the socio-technical system was seen to be acceptable by the population and the low-cost model was beneficial in low resource setting.

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I. INTRODUCTION

Increasing urbanization, environmental and lifestyle changes around the world combined with rapid demographic, sociocultural, and economic transitions led to the surge in non-communicable diseases (NCDs) in the past few decades[1]. The increasing prevalence can be attributed to behavioural and biological risk factors like use of tobacco, alcohol, physical inactivity and obesity.The incidence of NCDs like diabetes, cardiovascular disease, chronic lung diseases, and cancer are skyrocketing, with a staggering 71 percent of global deaths due to NCDs.[2] To increase availability of NCD services directly to more people and decrease the inability to pay for the screening services for NCDssmart digital tools can be used to deliver quality health care services at doorstep. Early identification, self-care interventions, community mobilisation, and

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health education are identified as low cost solutions to reduce the NCDs.[3]

The government's ability to limit the burden of NCDs limited owing the diverse socio economic and cultural issues spread regions in India. TheMinistry of Health and Family Welfare has initiated action on many fronts, such as introduction of National Action Plan and Monitoring Framework for Prevention and Control of NCDs, m-Diabetes, digital and broadcast media campaigns, reduction measures for the harmful use of tobacco and alcohol, community based screening of NCD's, among others.[4] In 10 years Diabetes, heart disease and stroke cost India US$ 237 billion (2005 to 2015). India is estimated to lose US$ 6.2 trillion due to NCDs during the period 2012-2030, whereas India could lose US$ 4.8 trillion in lost economic output by 2030 due to NCDs.[5]

Healthcare systems often face challenges with limited resources that restrict the reach of the healthcare services to the last individual. The gap to address these challenges increases in the under-developed and developing countries.[6] There is need for innovative solutions to respond to the challenges the public health is facing today. Non communicable disease screening in India had been a challenge given the public health force is completely dedicated and occupied with Reproductive and family planning services and the current pandemic services [7]. India had spent 13,200 crores under CSR act in the financial year 2018-2019 of which 38.6% is spent under education and health related sectors.[8]

II. MATERIALS AND METHODS

A socio-technical approach was adopted for the population based NCD screening program. The model leverages technological developments in the space of point of care tests to make screening services available to the larger population. Technology acts as the bridge that makes screening services available and accessible to deprived populations. It is widely acknowledged that adopting a socio-technical approach to system development leads to systems that are more acceptable to end users and deliver better value to stakeholders.[9]

Technology acts as the interface that helps the organization to materialise its driving factors to a process that helps society overcome its limiting factors. Technology also aids in addressing overlying systemic challenges that exist in the broader environment of NCD screening.

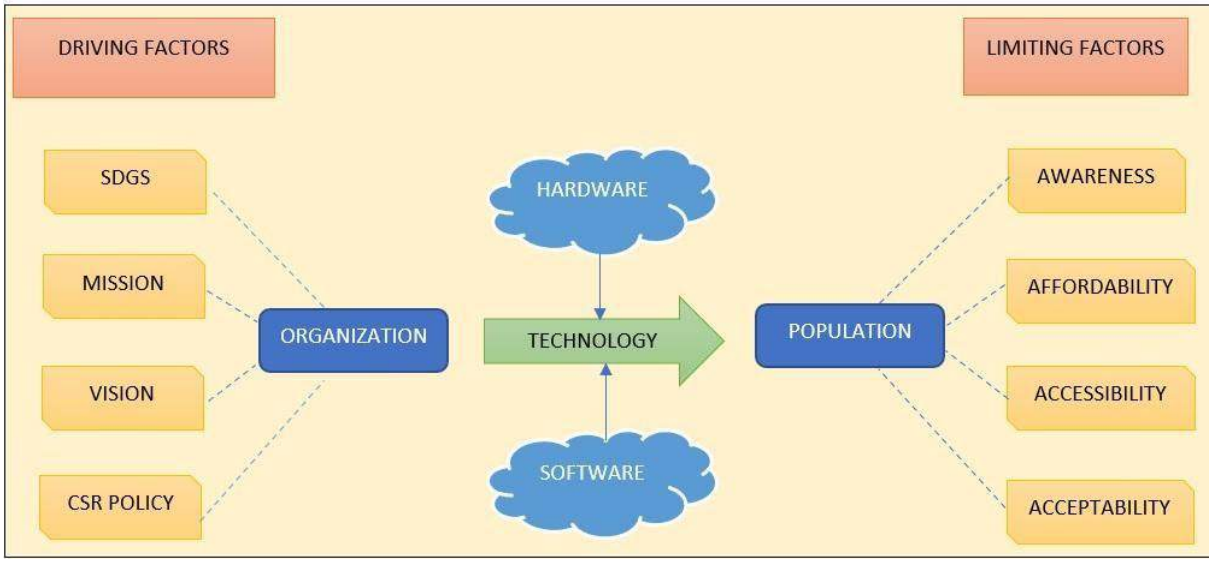

Figure 1: Conceptual Framework of Socio-Technical approach for NCD screening

The socio-technical structure considers the human, social and organisational factors as well as the contributing technological factors. This NCD screening model discusses how technology

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was used to link the motivating factors of the organization to address the limiting factors of the general population thus establishing a socio -technical system for NCD screening. 'Socio' refers to both the implementing organisation, the stakeholders as well as the benefactors while technology takes on the challenge of meeting their requirements and objectives.

Organization: NCDs pose a major risk to the health of the nation and the health systems. While the government has launched programs targeted towards reducing the mortality and morbidity due to NCDs, several other non-profits as well as corporates through their CSR have dedicated efforts to achieve the same goal. Sustainable Development Goal 3.4 targets to reduce premature mortality due to NCDs by a third by 2030. [10]

The CSR law mandates all organizations with net worth of 500 crore or 1000 crore turnover or 5 crore profitto spend 2% of their last three years and the social impact of the spend should be captured through measurable indicators.[11] This law mandates all organizations falling the purview of the above conditions to identify the gaps and address them through scalable and sustainable solutions.This helped us to develop this model to deliver high quality affordable healthcare services to the broader population. Through the aegis of CSR, we engaged in population-based preventive and screening activities.Narayana Health during the same financial year spent 21.2% of its total CSR expenditures in NCD Program[12] of which 5% was used in the present study. It was envisioned that the program identifies an acceptable solution for population screening in a low resource setting. The team was formed, and the objectives were laid out to understand the gaps in existing healthcare delivery and develop solutions that are scalable in low resource setting.

Population: The target population for the screening program were people from deprived/low resource settings. The program activities focused on rural and urban slum locations. A pilot project conducted in Bangalore found that awareness regarding NCDs was low. Prevalence of NCDs in the pilot population was found to be 29%.[13]Poor access to screening and general healthcare facilities was one of the major limiting factors to getting screened for NCDs. The cost involved in getting tested/screened was another deterring aspect. When the service was made available, issues related to acceptability arose, low acceptability to screening facilities was found to be associated with the low levels of awareness.

Technology: The technology system designed and developed comprised of various hardware devices that use different software applications to give immediate results. These devices were assembled into a kit that could be operated by frontline healthcare worker. The NCDs targeted through the intervention included diabetes, hypertension, cardiac disorders, anaemia, breast cancer and oral cancer. Family history, habit history and other demographic details are also factored in the screening process to gain better understanding of risk. Learnings from the pilot were crucial in enhancing and customising the technology and system for screening NCDs. As helpful as technology is, it does not solve problems on its own — it is only as good as its implementation. This can be achieved by marrying human values with the specific technological solutions .

Hardware & Software: The community needs were understood by secondary data research and an NCD screening app was developed to screen the NCDs prevalent in the community through point of care devices. Point of care medical devices with AI interpretation were used to screen NCDs. The Major NCDs screened and the devices used

Blood Pressure – Non-Invasive Blood Pressure (NIBP) device

Electronic BP devices. Non-Invasive Blood Pressure devices are used to measure and display arterial BP by automated and semi-automated inflation and deflation of a cuff applied to an extremity and through oscillatory method by transducing vibrations into electrical signals produces a digital readout of systolic and diastolic pressures.[14]

Hemoglobin - Hemoglobinometer

Hemoglobin - Hemoglobinometer

Small handheld hemoglobin analyser with less than 2 seconds measuring time used as a point of care device. A fast ergonomic and easy to use portable device is used to measure the HB levels in the blood. The device uses photometric azide methaemoglobin method to assess the HB using the reagent free cuvette with unique design and uses only one drop of blood needed.[15]

Blood Sugar - Glucometer

The device uses glucose dehydrogenase/flavin dinucleotide chemistry, automatic test strip calibration, and auto compensation for haematocrit. The strip requires a small blood sample (0.6 µl), and its test strips have a separate electrode that measures haematocrit so that the meter reports a haematocrit-compensated BG. Results are available in 8 seconds. A test strip that collects 0.6 µl through capillary method and the results and are displayed on the screen in 8 seconds.[16]

Weight - Weighing scale

Digital scales work with the use of a strain gauge load cell. Whereas analog scales use springs to indicate the weight of an object, digital scales convert the force of a weight to an electric signal. The weight of the person can be recorded in different measurement scales like lbs, Kgs, Pounds etcs. [17]

Height - Digital height device

The device used to measure the height digitally uses the ultrasonic method to estimate the height in centimetres and meters. [18]

SP02 - Pulse oximeter

The oximeter utilizes an electronic processor and a pair of small light-emitting diodes (LEDs) facing a photodiode through a translucent part of the patient's body, usually a fingertip or an earlobe. Oximeters operate based on this principle of different absorption and light emission. *[19]*

ECG – 6 lead ECG

An electrocardiogram (ECG) is a recording of the heart's electrical activity. It is totally painless and can be performed quickly. The heart's electricity is detected by adhesive electrodes attached to the skin. The resulting measurements are referred to as leads and uses Ethiopiantriangle to assess the ECG and the AI interpretation is done using Glasgow algorithm. The leads were colour coded and labelled to reduce confusion. The leads come with clamps are attached to fore-arms and legs. [20]

Vision (Refractive Index) - Phoropter

A low-cost folding phoropter was used to understand the prevalence of refractive errors in the population.[21]

Breast Cancer screening

Clinical breast examination and a Handheld device was used to screen for breast cancer. The frontline health worker was trained in CBE for 3 months under an oncologist. The handheld device uses pressure mapping to detect lumps in the breast through its sensors.

Oral Cancer screening

The frontline health care worker was trained to identify the precancerous lesions in the oral cavity. He also takes the pics on field and uploads them on the dashboard for diagnosis by the oncologist at a later stage.

Tablet with NCD app

An app was developed to ease the process of data collection and decision making in the field. The app interface was easy to use and the segregation of the app into pages for demographics, Past medical history, Habit history and Vitals with underlying condition to minimize data entry errors. The back end has dashboard with infographics to segregate the high-risk individuals for referral to public health institutions.

The following criteria were taken into consideration while selecting devices to perform tests:

- Certification and approval by agencies and authorities
- Point of care yielding immediate results
- Portable light-weight devices
- Field hardy
- Long battery life
- Easy to use and interpret results

Figure 2 and 3: NCD kit with Handheld breast cancer screening device and back pack with point of care device

III. RESULTS

Through the NCD program a total of 16,635 individuals have been screened, camps were organized with 63factories/NGOs/civil societies etc,. A team of 4 people were working for 6-8 hrs a day with 1-hour lunch break and two 15 min tea break. A CSR budget of 10,00,000was spent to screen the 16635 individuals that includes HR cost, Travel, and food expenses which translates to 60 rupee per beneficiary.

Task/Outcomes

Between June 2019 and January 2020 over 16000 individuals were screened for major NCDs at the communities, factories, urban slums, villages etc., The following indicators were monitored to assess the program

No of screening camps done -198
No of organizations approached -45
No of health awareness session – 78
No of breast cancer screening done -6538
No of Mammograms done (for suspected) – 1299
No of breast cancer cases – 02 (1 benign and 1 IInd stage cancer)

Between June 2019 and January 2020 over 16000 individuals were screened for major NCDs at the communities, factories, urban slums, villages etc., of these 32% (5335) were men and 68% (11300) were women. High BP was found in 22.6% (3757) respondents of which 29.8% (1121) were unaware of their condition. Diabetes was found in 9.1% (1522) and prediabetes was found in 5.5% (924) participants of which 37.2% (911) were unaware of their high blood sugar levels. The prevalence of hypertension among the men 30.9% (1650 out of 5335) and women 18.6% (2107 of 11300) was below the average national prevalence. The prevalence of Diabetes among the men 12.3% (661 out of 5335) and women 7.6% (861 of 11300) was above the average national prevalence. There were 25.1% overweight (BMI -25-30) and 7.8% obese (BMI >30) individuals in the study. Anaemia was prevalent in 36.4% (n= 6057) individuals of which 32.3% (n=5386) were mild anaemic, 3.4% (n=574) were moderate anaemic and 0.48% (n=97) were severe anaemic.

Table 1: Prevalence of major NCDs among the population screened

Vitals (N=16635)		Males (N=5335)	Females (N = 11300)	Total prevalence (N=16635)	Individuals not aware of their underlying condition
High Blood Pressure	Systolic	9.9%(n=1650)	12.6% (n=2107)	22.6%(n=3757)	1121
	Diastolic	3.2%(n=535)	2.4% (n=405)	5.6%(n=940)	694
Diabetes	Pre-Diabetes	2.3%(n=387)	3.2%(n=537)	5.5%(n=924)	
	Diabetic	3.9%(n=661)	5.1%(n=861)	9.1%(n=1522)	911
Body Mass Index	Overweight	7.8%(n=1312)	17.2% (n=2867)	25.1%(n=4179)	
	Obese	2.3%(n=397)	5.5%(n=914)	7.8% (n=1311)	1200
Anaemia	Mild	4.6%(n=770)	27.7%(n=4616)	32.3%(n=5386)	5386
	Moderate	0.3% (n=51)	3.1%(n=517)	3.4% (n=574)	574
	Severe	0.08%(n=14)	0.4%(n=83)	0.48%(n=97)	97
ECG	Referred	0.06%(n=11)	0.08% (n=14)	0.15%(n=25)	25
Oral Cancer screening	Follow up	5.19% 864	5.53% 920	10.7% 1784	1784
	Pre-Cancerous lesions	0.25% (n=42)	0.27% (n=46)	0.58% (n=98)	98
	Oral cancer	0	1	1	1

Follow-up with identified high-risk cases is an important aspect of this initiative and is necessary to complete the loop of this process. 80% of the respondents who were identified as high risk were followed-up with at least thrice. Follow up is done by the frontline healthcare workers through a call. The person is encouraged to adopt lifestyle modifications and seek treatment at their nearest healthcare facility.

IV. DISCUSSION

The results from NCD screening solution showed the desired outcomes the potential of the model to substitute the disease screening programs in a low resource setting. The emerging technologies in medical field and their complexity in adapting to a low-cost solution is addressed using a socio-technical system. The observations from the implementation of the NCD screening program helped us in understanding the community needs, user experiences and the continuing change to address the emerging needs.

4.1 People

The interaction between people and technology is important for any solution to reach its objectives. The following people from the program implementation were interacting with the technology

4.2 Frontline Health workers

The screening solution was developed to equip the frontline health workers with an innovative kit that would screen all the four major non communicable disease conditions. The kit interface was developed such that even a person with minimal technological understanding can use it efficiently. The NCD screening kit interacts

with the program personnel, end user and beneficiary to increase time efficiency, conditional clauses to reduce errors in data entry, new age medical devices that uses AI interpretations, decision making through interactive visualization, empowers the frontline health workers in NCD screening. Each NCD kit was operated by three front line healthcare workers in the camp to reach out to the maximum number of beneficiaries. A team each with three healthcare workers, a camp coordinator and two kits over a period of 6 months were able to reach out to 16335 beneficiaries.

1. Consent form collection
2. Weight measurement
3. Height measurement
4. Waist and Hip measurement
5. Blood pressure recording
6. Pulse oximeter recording
7. 6 lead ECG recording
8. Hemoglobin reading
9. Blood sugar reading
10. Oral cancer examination
11. Thermal print out of results
12. Explaining the results

4.3 Beneficiaries

The target population was from low socioeconomic background who are usually missed out in the screening drives conducted by the government health workers. The groups were reach out by organizing camps in the urban slums, villages, Industrial areas, in collaboration with the microfinance organizations and NGOs working with the marginalized. A total of 16,335 beneficiaries are screened for Non communicable diseases of whom 11300 were females and 5335 were males. The average age of the beneficiaries was 40.1 years and 90% of them have never been screened all the major NCDs.

4.4 Camp coordinator

Monitoring and evaluation were carried out through NCD screening app that synchronizes data to the dashboard where through data visualization the high-risk individuals were identified and reached. The coordinator also monitors the number camps being conducted and the beneficiaries reached each week.

4.5 Technology & Time efficiency

One of the major obstacles in NCD screening is the time and effort involved in screening everyone. If the waiting time is longer then it is difficult to reach more beneficiaries and the cost per screening also increases decreasing the traction to the program. To decrease the time per screening we have leveraged on technological and process innovation. Leveraging on technology we were able to get the HB results in 2seconds, Blood sugar results in 8 seconds, Blood pressure in 40 seconds, ECG in 45 seconds. Each frontline health worker with a single kit takes approximately 7.45minutes to screen one person which is ideal for house to house screening. Though this model could benefit the frontline health workers of LMIC it may not be acceptable in community screening due to increased waiting time as large number of people gather to get screened. Different process was tried and tested and was found out with additional 2 staff the screening time per individual can be drastically reduced to 3 minutes.

4.6 Interactive Visualization for decision making

The results were displayed on the tab in color coding as red, yellow and green indicating severe risk, moderate risk and no risk, respectively. This helps the frontline workers to identify the high-risk individual and refer them to the nearest health center. The results were then printed on to a 2-inch roll that contains the reference range, and the high-risk values are bolded. At the backend, the program personnel can print out the results for the area or location and the inbuilt programs gives out the results as mild, moderate and severe on five disease conditions.

V. CONCLUSION

NCDs are the major causes for mortality and morbidity across the world and in India. The healthcare services available for the public for early identification of NCDs in India remain unreachable to large sections of the community. The proposed NCD solution hopes to address the challenges in accessibility and affordability by reducing the time of screening and cost involved.

The portability of the kit enables the screening to be conducted at the convenience of the individual through multi stakeholder alignment.

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Transient Red Cell Aplasia Following Acute Human Parvovirus B19 Infection in a Sickle Cell Disease Patient in Aplastic Crisis

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ABSTRACT

Parvovirus B19 (PVB19) is a DNA virus, non-enveloped, with icosahedral nucleocapsid symmetry and measures 22-24 nm in diameter. Transmission is via blood transfusion being one of the transfusion transmissible viruses though infection can occur spontaneously. It is a major disease patients and Thalassemia patients, with clinical manifestation ranging from asymptoma- tic disease in immunocompetent to symptomatic disease in the immunocompromised. At risk group include children, pregnant women, immunocompromised and those with chronic haemolytic anemia. Clinical features include erythema infectiosum (fifth disease) in children, arthropathy, aplastic anemia/crisis and fetal hydrops.

Acute parvovirus B19 infection can be diagnosed by demonstrating the presence of HPV B19 IgM, with or without positive IgG using enzyme immunoassays (EIAs). Evidence of past infection is the presence of HPVB19 IgG. Red cell aplasia can be defined as a fall in haemoglobin concentration to below steady-state levels of more than 30g/l associated with a very low reticulocyte count.

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ABSTRACT

Parvovirus B19 (PVB19) is a DNA virus, non-enveloped, with icosahedral nucleocapsid symmetry and measures 22-24 nm in diameter. Transmission is via blood transfusion being one of the transfusion transmissible viruses though infection can occur spontaneously. It is a major disease patients and Thalassemia patients, with clinical manifestation ranging from asymptomatic disease in immunocompetent to symptomatic disease in the immunocompromised. At risk group include children, pregnant women, immunocompromised and those with chronic haemolytic anemia. Clinical features include erythema infectiosum (fifth disease) in children, arthropathy, aplastic anemia/crisis and fetal hydrops.

Acute parvovirus B19 infection can be diagnosed by demonstrating the presence of HPV B19 IgM, with or without positive IgG using enzyme immunoassays (EIAs). Evidence of past infection is the presence of HPVB19 IgG. Red cell aplasia can be defined as a fall in haemoglobin concentration to below steady-state levels of more than 30g/l associated with a very low reticulocyte count.

This was a case report of a 15 year old girl, a known sickle cell anemia patient (HbSS) diagnosed a year after birth and has been stable on folic acid. Routine follow-up clinic visit has been irregular as patient had been clinically stable and crisis free on till about 15 months prior to presentation at our centre. Her steady state PCV hence could not be ascertained. She however started having extreme fatigue, tiredness and easy fatigability about 15months prior to her referral to our centre. On examination she was found to be severely pale with PCV of 6%. This necessitated her been transfused with whole blood at the peripheral health centre where she was been managed. PCV improves post transfusion for a few days after which the patient starts having dark coloured urine, jaundice, bone pains and generalized body pains. subsequently, the PCV drops to pre-transfusion level or below necessitating her frequent transfusion, atleast twice a month for upto 8 months before her referral to a tertiary health centre for further investigation.

Investigations done include CBC, PBF, BMA, repeat haemoglobin genotyping using HPLC G6PD assay and Human Parvovirus B19 screening. Findings were in concordance with aplastic anaemia, negative for G6PD deficiency but was positive on screening for HPVB19 with a high persistent fetal hemoglobin of upto 31%.

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I. INTRODUCTION

Parvovirus B19 (PVB19) is a DNA virus belonging to the parvoviridae family and of the erythrovirus genus (1). Alongside hepatitis B virus (HBV), hepatitis C virus (HCV), human immunodeficiency virus (HIV), human T cell leukaemia virus I (HTLV1), cytomegalovirus (CMV) and Epstein -Barr virus (EBV), It is another transfusion transmissible viruses. It is non-enveloped, with icosahedral nucleocapsid symmetry, and measures 22-24 nm in diameter. The virus has a linear nucleic acid (DNA) of ~5.6 kb in length with three (3) genotypes 1, 2 and 3. Genotype 1 had been implicated for the majority of human infections worldwide while genotypes 2 and 3 appear to have some geographic and temporal variation in distribution. The strength of them virus is seen in its resistant to dry heat, freezing and lipid solvents but can be inactivated by formalin, β-propiolac tone and gamma irradiation (2).

The main transmission route of the virus is as droplet infections, vertically through placental to fetus and through blood transfusion. The population at risk include children, pregnant women, immunocompromised and those with chronic haemolytic anemia such sickle cell and Thalassemia patients (1,3), with clinical manifestation ranging from asymptomatic disease in immunocompetent to symptomatic disease in the immunocompromised. Clinical features include erythema infectiosum (fifth disease) in children, arthropathy, aplastic anemia/crisis and fetal hydrops (2).

Acute infection is associated with a viremic phase shortly followed by IgM antibody production (10–14 days post-infection). This is followed by IgG antibody production against the viral capsid. Viraemia declines with IgM production; IgM declines after a few months but IgG persists longer to convey immunity against reinfection. Infrequently, low level PVB19 nucleic acid may persist with IgG for months or years (2).

Parvovirus B19 infections has been reported globally and are evident with the secretion of immunoglobulin M (IgM) antibodies in plasma while IgG signify previous exposure. The clinical manifestation varies widely depending on the immunological and haematological status of the host as the virus has a direct cytopathic effect on erythroid progenitors in bone marrow leading to an arrest in the maturation and subsequent anaemia. According to Serjeant *et al.,* individuals with underlying haemolytic disorders, such as patients with sickle cell anaemia (SCA), PVB19 infection may cause transient erythroblastopenia (TEB), characterized by a fall in haemoglobin level with reticulocytopenia (4). Other manifestations of parvovirus infection include arthritis, vasculitis, myocarditis, liver failure and fetal loss (2). SCA patients have accelerated premature haemolysis with significant reduction in red cell half life (5). Generally, the chronic haemolysis and resulting anaemia is well tolerated however, a reduction in the level of haemoglobin below the steady state may be detrimental to the patient; necessitating blood transfusion (6, 7).

Transfusion predisposes SCA patients to increased risk of immunological and infectious complications and accurate epidemiologic data on the frequency of Parvovirus B19 infection in patient with sickle cell anaemia are essential for assessing the potential effect of viral prevention programs in this patient population (8). Though the findings from the work of Iheanacho *et al.* (2014) suggests that it may not be cost effective to recommend routine donor screening for PVB19 antibodies. However, because of the increased risk of aplastic crisis in SCA patients, SCA patients who require transfusion and are seronegative for PVB19 should have the blood screened for PBV virus. We hereby present a case of a 13 year old sickle cell anaemic girl with PVB19.

II. CASE REPORT

Patient was a 15-year-old female with HbSS and infrequent admissions and had never received any previous blood transfusions prior to this episode of ill health as she has been clinically stable on folic acid. her steady-state PCV could not be ascertained due to irregular follow-up clinic visit. In February 2019, she presented with lethargy, easy fatigability and dyspnoea. she was extremely pale with a PCV of 6%. She was managed supportively with blood transfusion.

complete blood count following transfusion showed the following: PCV (28.1%), Haemoglobin (10.0g/dL), white blood cell (1,200/cmm^3), platelets (59,000/cmm^3), lymphocyte (59.6%), neutrophils (35.3%), Baso, Eos, Monocytes (5.1%), Red blood cell (3.53 *10^{12}/L), MCV (79.8fL), MCH (28.3Pg), MCHC (35.5g/L) and PCT (0.04%). Few weeks post transfusion, she presented at the private health facility where she is being managed with extreme weakness, passage of dark coloured urine, jaundice and generalized body pains. Her complete blood count showed PCV (9.1%), Haemoglobin (2.9g/dL), white blood cell (1,600/cmm^3), platelets (60,000/cmm^3), lymphocyte (68.9%), neutrophils (27.2%), Baso, Eos, Monocytes (3.9%), Red blood call (0.92 *10^{12}/L), MCV (99.0fL), MCH (31.5Pg), MCHC (31.8g/L) and PCT (0.06%). She was transfused with 2 units of whole blood on account of this. The cycle of low PCV, blood transfusion, relapse of anaemic crisis continued, necessitating her being transfused atleast once every month for upto 8 months before her referral to a tertiary health Centre for further management.

At admission, her haemoglobin genotyping was repeated using HPLC revealed a foetal heamoglobin (31.8), haemoglobin A0 (26.4), haemoglobin A2 (1.6), haemoglobin S (40.2). Further investigations carried out include Complete Blood Count with Peripheral Blood Film which revealed pancytopaenia. Bone Marrow Aspirate and cytology was also done which showed hypocellular marrow. Other tests carried out include G6PD assay which was within reference range of activity (247 mU/10^9 erythrocyte), as well as Human Parvovirus B19 screening which was positive for HPV B19 DNA in blood using Parvo virus B19 DNA test.

III. TREATMENT

Patient was managed conservatively with methylprednisolone (32mg/dl), cyclophosphamide (100 mg/dl) and immune boosters such as glutathione supplementation and selenium-based therapy.

IV. OUTCOME AND FOLLOW-UP

Patient recovered from acute haemolytic episode with remarkable increase in PCV and a reduction in the frequency of transfusion. She was transfused once in the last four months and has returned back to school and normal activity, maintained on the present line of supportive care.

V. DISCUSSION

Parvovirus B19 is one of the emerging transfusion transmissible infections. Interventions for parvovirus B19 infection need to balance the low risk of infection at a population level with the potential for serious adverse outcome for particular groups, notably the fetus, people with haemoglobinopathies and the immunocompromised. The virus is stable in heat and remains infective even after treatment with dry heat at 80°C for 72 hours, which was used for treating some blood products (9, 10).It has been widely studied in various countries among healthy blood donors and sickle cell patients with results indicating a high seroprevalence of the virus in the study areas however there are limited publications on parvovirus in SCA patients and blood donors in our environment. Iheanacho (2013) reported a seroprevalence rate of 66% for IgG antibody in Nigerian healthy blood donors (2). Abraham et al and Munoz et al reported seroprevalence of 65% each for IgG antibody in blood donors in India (11) and Salamanca, Spain (12) respectively. In various studies in developed nations, rates between 55 – 77% were reported (13–15). In non-immune sickle cell anaemia patients, the clinical manifestation of the virus upon infection may include transient aplastic crisis, which is indicated by a fall in haemoglobin with reticulocytopaenia. Serjeant et al in their study of epidemiology of human parvovirus B19 infection in Jamaica in homozygous sickle cell disease found that PVB19 infection account for most if not all aplastic crisis in SS disease (4). The reticulocyte percentages of IgG antibody positive SCA patients are generally higher than that of IgM positive SCA subjects. This affirms the risk of transient aplasia associated with acute or persistent parvovirus infection documented in some previous studies (16). A high seroprevalence

of IgG anti-PVB19 antibodies in sickle cell patients and voluntary blood donors in our environment had been reported. This suggests that it may not be cost effective to recommend routine donor screening for PVB19 antibodies. However, because of the increased risk of aplastic crisis in SCA patients, SCA patients who require transfusion and are seronegative for PVB19 should have the blood screened for PBV virus.

VI. CONCLUSION

The high seroprevalence of IgG anti-PVB19 antibodies in sickle cell patients and voluntary blood donors in our environment suggests that it may not be cost effective to recommend routine donor screening for PVB19 antibodies. However, because of the increased risk of aplastic crisis in SCA patients, and severe complications which may occur following the infection such as nephrotic syndrome and progressive renal fibrosis, SCA patients who require transfusion and are seronegative for PVB19 should have the blood to be transfused screened for Parvovirus B19. The discovery of this case hereby calls for intentional approach to parvo-virus B19 (2). Severe complications associated with acute HPV B19 infections in patients with SCD supports the development of HPV B19 prevention strategies, targeting particularly patients who are still HPV B19-naïve.

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