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Article

The Influence of Parental Environmental Exposure and Nutrient Restriction on the Early Life of Offspring Growth in Gambia

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Abstract: Background: The trends in the role of the germline in epigenetic transgenerational inheritance starts with the environmental factors acting on the first generation of a gestating mother. These factors influence the developing second-generation fetus by altering gonadal development, thereby reprogramming the primordial germ cell DNA methylation and leading to consequences that would be seen along generations. **Objective**: Despite these epigenetic factors now surfacing, the few available studies are on animal-based experiments and to make follow up on human intergenerational trials might take decades. To this response, this study aimed to determine the influence of parental energy, toxicant exposure, age and nutrient restriction on the early life of offspring growth in Gambia. **Method:** The study was on population-based observational study on parental energy influence, toxicant exposure, age, and nutrient restriction on offspring growth in Gambia. **Results:** This study showed that parents who worked in industrial areas were more likely to have offspring with poor psychosocial skills. In addition, mothers who are exposed to oxidative stress

and high temperature are more likely to have offspring with poor psychosocial skills. Mothers who consumed a high protein diet were almost three more likely to have infants with good psychosocial skills in their offspring. Furthermore, there was a negative correlation between maternal stress during pregnancy and psychosocial skills of offspring. **Conclusion:** This study was able ascertain if maternal diet during gestation, toxicant exposure, maternal stress and parental smoking habits have influence on the early life of offspring. While the study is recommending a large sample size study to eliminate selection bias, there should be an increased level of awareness of mothers on their offspring's health and their husbands' lifestyles that might influence the adulthood health of offspring.

Keywords: Epigenetics; Toxicant exposure; Maternal stress; Parental smoking; Offspring health

Introduction

In addition to genetic influence, the environment can determine the health and well-being of progeny. A typical example is seen between identical twins whose DNA is very similar but has different levels of risks to various diseases due to environmental exposures [1]. While this influence is not entirely from DNA as spontaneous genetic mutations, epigenetic changes include alterations in DNA methylation status, the post-translational modification of histones and non-protein-coding RNA [2]. In addition to the genetic constitutions, which is DNA inherited by an organism, the trajectory in human development that led to mature phenotype are also determined by mechanisms acting during critical

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windows in early life. This influence was studied to establish stable patterns of gene expression [3]. Although this is not accounted for by variations in DNA sequence, it causes permanent phenotypic consequences for offspring like implications in psychological, developmental problems, stress response and immune functioning [4]. Furthermore, unlike genomics, epigenetic marks are reversible in nature. In a sense, multiple rounds of epigenetic reprogramming can completely erase the existing patterns. How these affect an individual's germline and how it can be transmitted to the preceding generations are the interesting questions genetics are yet to unearthed. This approach entails the combination of genetic and epigenetic modifications and the mechanism involved in determining the phenotypes of individuals and their offspring [2, 5].

The germline, which altered DNA methylation will become permanently programmed. Consequently, this imprinted-like gene will be passed down through the germline to subsequent generations [1, 2]. The developing embryo generated from this specific germline will be an altered epigenome, which may affect developing somatic cells and tissues. The integrated epigenetic modifications into the genome of individuals have the potential to modulate gene expression. In addition, it can modulate gene activity at enhancer and promoter domains [2]. Similarly, genetic mutations alter sequence availability for methylation and histone binding. These combinations are studied to present a stable inheritance feature or to the next generation or germline. These alterations to nuclear composition are due to environmental factors, ageing, diet and toxicant exposure and the likes [2]. Cytochrome P450 activity, gestational duration, maternal glucose, immune functions, smaller head circumference and the likely maternal blood pressure are all crucial for fetal growth and low and high birth weights to be specific [24]. Moreover, maternal blood pressure linked to offspring's low birth weight is strongly evident in genetics instead of an adverse intrauterine environment [26]. Prenatal exposure to earthquake results in earlier delivery in addition to reduced length and head circumference and this is relative to the trimester of exposure [27]

These risk factors for epigenetic changes are maternal undernutrition, hyperglycemia, birth weight, obesity, high-fat and low-protein diet and diabetes mellitus. Furthermore, advanced age, smoking, and environmental chemical exposure affect the offspring's metabolic and cardiovascular health later in life [6]. The emerging associating factors are paternal obesity, nutritional habits, diabetes mellitus status, advanced age and exposure to environmental chemicals or cigarette smokers. These are seen with episodes of adverse effects in metabolic and cardiovascular health in offspring [7]. Environmental chemicals alter hormone signaling or disrupt hormone production. This causes endocrine disruption, which has profound consequences on hormones' role in human development [1]. Nephrogenesis is impacted by poor placental function, inadequate diet, maternal stress, maternal smoking and alcohol consumption. A reduced nephron endowment with a high risk of developing hypertension and chronic kidney disease (CKD) may result in [8]. In addition to maternal nutrition, paternal periconceptional nutrition affects offspring's likelihood of developing chronic metabolic-related conditions and cardiovascular diseases due to epigenetic imprinting [9,10]. Moreover, maternal obesity affects the cognitive function and mental health of the offspring [11].

It is obvious that an improved diet plays a big role in general health and wellbeing. This is inconsistent with proper maternal nutrition during pregnancy. Monitoring the glycemic level will add up to maternal health and reduce the risk of later obesity of infants and the body composition [12]. For instance, around conception and in early pregnancy, insulin resistance and glycaemia affect fetal nutrient supply. Also, throughout gestation period, maternal-feto-placental communications will be affected. All these will reflect in the later postnatal health [12, 13]. Following the available nutritive diet during the period of early gestation through lactation, this study would be able to ascertain the evidence exposed *in utero* to famine and greater risk of poor health in later life [14]. In response to these epigenetic imprints, this study is designed to determine the influence of parental energy, toxicant exposure, age and nutrient restriction on the early life of offspring growth in Gambia.

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Methodology

Study design

The study was on population-based observational study on parental energy influence, toxicant exposure, age, and nutrient restriction on offspring growth. This observational study is associated with parental exposure to energy and nutrient restriction *in utero* on their children's growth in rural Gambia [13]. While the study proposed that under matriline influence, fetal growth and postnatal growth under patriline intergenerational influences only in one sub-district in Gambia, the current study is designed to combine both maternal and paternal factors across the country.

Study setting and duration

This study was conducted between August and October, 2021 in Gambia. Gambia is the smallest West African nation in mainland Africa and located on the western coast of Africa. It is long and narrow in shape, extending 487 km into the hinterlands, with an average width of 24 km. At the point where the River Gambia meets the Atlantic Ocean, the width of the country is twice the average at more than 48 km. The country is bound on three sides by Senegal and on the west by the Atlantic Ocean. The population of the Gambia is estimated to be 2.4 million [23].

Study population: This survey gives details including lifestyles and health details for reproductive mothers and their last born (child under 5 years).

Inclusion and exclusion criteria: Mothers with their last born at least under 5 years from all provinces across the Gambia meet the inclusion criteria. However, mothers who were recruited in taking supplements during pregnancy were excluded in this study.

Sample size

The minimum sample size is determined by using a single population proportion formula; $n = (Z\alpha/2)^2 * p\ (1-p)/d^2$). Whereas; n = the required sample size for this study; $Z\alpha/2(1.96)$ = significance level at α =0.05 with 95% confidence interval; p = proportion of reproductive women with a child under 5 years of age, which is estimated to be 25.2%; and d = margin of error (5%). Inserting values into the equation, the minimum sample size was 293. We finally recruited 339 respondents that includes the 10% non-response rate, missing and incomplete responses.

Data collection tools

Structured interview questionnaire was developed by the research team, which includes public health professionals, nurses and medical students of the University of Gambia conducted three months long interview by house visit while assessing the antenatal care (ANC) cards to supplement some information.

Data collection procedure

The interviews were conducted by trained public health officers, trained nurses and some student nurses and the information were filled online simultaneously. The authentication of some information was based on the consultation of the ANC card of the child in question. Regarding the geographical information system, the study was able to track the map as to how and where the data in relation to the participants were collected.

Data quality and bias mitigation

The questionnaires were pretested to about 5% of the estimated sample size to check for validity and reliability. The study questionnaires were administered by the research team. To avoid potential information bias, the study details including the questionnaire were explained to the participants if necessary. The completeness of each questionnaire was verified by the researcher daily.

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Data analysis

Data was analyzed using Statistical Package for Social Sciences (SPSS) version 23.0. Descriptive statistics was performed to calculate percentages, frequencies, range and mean for quantitative variables. Bivariate analysis was performed and only variables with p-value < 0.05 were declared statistically significant. Those that meet statistical significance were included in the multiple logistic regression analysis model to compute for adjusted Odds Ratio (aOR) at 95% CI (Confidence Interval). To be specific, Pearson product moment correlation and ANOVA was used to estimate relationships across selected study variables. Independent sample t-test was used to determine mean differences.

Ethical Issue

The researcher obtained approval from the Department of Microbiology at the Xiangya School of Public Health, Central South University and the RePubliC Committee at the School of Medicine and Allied Health Sciences, University of The Gambia. Informed consent was given to each participant to sign or thumb print depending on their preferences prior to recruitment into the study. The decision to sign the consent form is made by each participant without the researcher's interference. Participant's privacy and confidentiality were maintained throughout the study. Each of the study participants had the right to withdraw from the study at any point in time during the course of the study without their rights being infringed/affected.

Results

Socio-demographic characteristics of the participants

A total of 339 women participated in the study in which more than half (53.7%) were from western region. Kanifing Municipality Council accounts for 16.5% of the total participants followed by North Bank Region (12.4%). 98.8% of last-born children of the participants were alive in which majority are male (51%). On marital status of participants, 92.3% of the respondents were married and 4.7% were single. With regards to occupation, majority (72.3%) of the respondents (mothers) were housewives and occupation of fathers accounted for 62.5%. Furthermore, 78.2% of the participants resides in municipality regulatory area and 12.1% lived in moderate municipality regulatory area. On settlement type, majority (92%) lived in urban settlement. Majority of the respondents (56.6%) have in house bathroom and 42.2% had a short distance behind bathroom (Supplementary Table 1).

The average age of the respondents (mothers) was 29 years, father wass 39 years and average length of marriage was 9 years. The average age of the last child was 4 years. Average monthly income of the households was D6161.7 ± 27797.8, which is $100. Also, average number of people living in a household was 6, and number of children under-five was 1.

Psychosocial skills of offspring aged 3 to 5 years

Majority of the respondents' infants had good health profile or record. For example, only 11.8% of the respondents' infants were malnourish, 4.4% had low hemoglobin, 0.3% had sickle cell disease and 4.4% had asthma.

Neonatal complications can pose serious threats to the survival of the infant especially in the first 100 days. Our findings showed that 10.6% of the infants had poor suckling abilities, 15.9% had fever, 5.6% had breathing problems and 8.96% had low birth weight.

Frequency analysis showed that 39.2% of respondents' offspring had very good social skills and 33% had excellent social skills. On communication skills, 37.6% of the respondents' offspring had very good skills followed by 30.6% with good skills on average. 35.3% had good cognitive skills followed by 28.8% with excellent cognitive skills. With regards to motors skills 31.8% had excellent skills. On activities of daily living, 38.3% had excellent skills (Table 1).

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Table 1. Psychosocial skills of offspring between 3 to 5 years (n=339).

Psychosocial skills	Poor (%)	Good (%)	Very Good (%)	Excellent (%)
Social skills				
Eye contact	3(0.9)	91(26.8)	141(41.6)	104(30.7)
Joint attention	4(1.2)	102(30.1)	136(40.1)	97(28.6)
Responding to adult direction	2(0.6)	69(20.4)	142(41.9)	126(37.2)
Recognize emotional states	3(0.9)	137(40.4)	84(24.8)	115(33.9)
Peer friendships	0(0.0)	61(18.0)	161(47.5)	117(34.5)
Average scores	**0.7**	**27.1**	**39.2**	**33**
Communication skills				
Shift gaze of person to object	20(5.9)	127(37.5)	117(34.5)	75(22.1)
Gesturing	2(0.6)	102(30.1)	154(45.4)	81(23.9)
Pointing	2(0.6)	75(22.1)	131(38.6)	131(38.6)
Expression of emotions	5(1.5)	111(32.7)	108(31.9)	115(33.9)
Average scores	**2.2**	**30.6**	**37.6**	**29.6**
Cognitive skills				
Readiness skills	8(2.4)	135(39.8)	111(32.7)	85(25.1)
Object permanence or recalling	29(8.6)	106(31.3)	101(29.8)	103(30.4)
Smartness (Concept development)	28(8.3)	92(27.1)	107(31.6)	112(33.0)
Decision making	45(13.3)	145(42.8)	58(17.1)	91(26.8)
Average scores	**8.2**	**35.3**	**27.6**	**28.8**
Motor skills				
Gross motor	29(8.6)	129(38.1)	77(22.7)	104(30.7)
Playing on playground equipment	0(0.0)	61(18.0)	137(40.4)	141(41.6)
Jumping	10(2.9)	59(17.4)	166(49.0)	104(30.7)
Ball catching	69(20.4)	108(31.9)	79(23.3)	83(24.5)
Walking up/downstairs	31(9.1)	144(42.5)	58(17.1)	106(31.3)
	8.2	**29.6**	**30.5**	**31.8**
Activities of daily living				
Independent feeding	4(1.2)	114(33.6)	67(19.8)	154(45.4)
Toilet training	36(10.6)	69(20.4)	99(29.2)	135(39.8)
Clothes on/off independently	22(6.5)	74(21.8)	124(36.6)	119(35.1)
Hand-washing abilities	36(10.6)	123(36.3)	69(20.4)	111(32.7)
	7.2	**28**	**26.5**	**38.3**

Note: figures in brackets are in percentages.

Health profile of mothers preconception and during intra-partum and postpartum period

The health profile of mothers during intra-partum and postpartum showed 79.1% had normal labour, 90.6% had normal delivery, 77.3% had no excessive hemorrhage and also 7.4% experienced eclampsia. Majority (66.4%) of the respondents practiced exclusive breast feeding. See table 11 for more details.

Majority complained of early morning vomiting (66.4%) and breast engorgement. 28.6% had history of low hemoglobin and 11.2% had chronic high blood pressure. History of STI accounted for 8.3% of the respondents (Table 2).

Table 2. The health profile of the mother during preconception and conception (health profile including obstetric and medical histories).

Disease/conditions	No	Yes
Was there a miscarriage?	292(86.1)	47(13.9)
Early morning vomiting	114(33.6)	225(66.4)
Breast engorgement	275(81.1)	64(18.9)
Missed Period	82(24.2)	257(75.8)
Edema	317(93.5)	22(6.5)
Chronic high blood pressure	301(88.8)	38(11.2)
History of low hemoglobin (anemia)	242(71.4)	97(28.6)
History of sickle cell disease	331(97.6)	8(2.4)
History of STI	311(91.7)	28(8.3)
Diabetes mellitus	333(98.2)	6(1.8)
Diabetes mellitus (father)	330(97.3)	9(2.7)
Lung cancer (mother)	339(100.0)	0(0.0)
Peptic ulcer diseases	312(92.0)	27(8.0)
Paternal obesity	301(88.8)	38(11.2)
Lung cancer (father)	336(99.1)	3(0.9)

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Asthma	320(94.4)	19(5.6)
Tuberculosis	338(99.7)	1(0.3)

Smoking habit as predictors to the psychosocial skills of offspring

According to respondents, 21.5% of their spouses ever smoke and only 6.5% worked in industrial area. 18.3% of the male counterparts are active smokers and 9.7% of them smoke at home.

The univariate and multivariate analysis showed no association between smoking habit of parents and the psychosocial skills of their offspring. However, parents or fathers who worked in industrial areas were more likely to have offspring with poor psychosocial skills [OR=5.763(95% CI; 1.907, 17.414), p=0.002] (Table 3).

Table 3. Smoking habits as predictors of psychosocial skills of offspring.

Variable	No.	Unadjusted OR* (95% CI)	p-value	Adjusted OR (95% CI)	p-value
Father ever smoke					
	No (307)		Ref		
	Yes (32)	1.439(0.856, 2.419)	0.117	0.91(0.36, 2.303)	0.842
Father working at Industrial area (pollution)					
	No (317)		Ref		
	Yes (22)	5.763(1.907,17.414)	**0.002***	4.832(1.5, 15.563)	**0.008***
Active smoking parent					
	No (277)		Ref		
	Yes (62)	1.52(0.874, 2.644)	0.138	0.981(0.342, 2.816)	0.972
Parent smokes in house					
	No (306)		Ref		
	Yes (33)	1.898(0.911, 3.953)	0.087	1.246(0.339, 4.577)	0.741
Parent smokes around you while you are pregnant					
	No (306)		Ref		
	Yes (33)	1.898(0.911, 3.953)	0.087	1.231(0.368,4.123)	0.736
Smokes before and now quits					
	No (266)		Ref		
	Yes (73)	2.068(0.977, 4.379)	0.058	1.574(0.656, 3.773)	0.309

OR = Odds Ratio and CI = confidence interval, * Statistical significance.

Chemical exposure as predictors to psychosocial skills of offspring

Exposure to chemicals by parents especially the mother can predispose the infant or fetus to some medical complication. 60.5% of our respondents were exposed to insecticides, DDT, mosquito spray or coil; 70.2% to heterocyclicamines and 79.9% to Aflatoxin. Also, about 24.5% of the respondents reside by the roadside.

Table 4 shows univariate and multivariate analysis to predict factors associated with psychosocial skills. The analysis revealed that mothers who exposed to oxidative stress were more likely have offspring with poor psychosocial skills [OR=0.411(95% CI, 0.212, 0.796), p=0.008]. Also, mother exposed to high temperature were more likely to have offspring with poor psychosocial skills [OR=0.43(95% CI; 0.273, 0.679), p=0.001].

Table 4. Exposure to chemicals and psychosocial skills of offspring.

Variable	Category	Psychosocial skills		Unadjusted OR (95%CI	p-value	Adjusted OR (95% CI)	P-value
		Poor(n)	Good(n)				
Insecticides, DDT, mosquito spray or mosquito coil							
	No	65	69	Ref			
	Yes	117	88	0.709(0.458, 1.097)	0.123	0.707(0.442, 1.13)	0.147
Heterocyclicamines (2-cooked meat products)							
	No	46	55	Ref			
	Yes	136	102	0.627(0.393, 1.002)	0.051	0.871(0.515, 1.471)	0.604
Aflatoxin (eating too much peanut soup)							
	No	37	31	Ref			
	Yes	182	157	1.037(0.608, 1.768)	0.893	1.507(0.845, 2.686)	0.165

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Oxidative stress						
No	147	143	Ref			
Yes	35	14	0.411(0.212, 0.796)	**0.008***	0.521(0.282, 1.06)	0.072
High Temperature						
No	97	114	Ref			
Yes	182	157	0.43(0.273, 0.679)	**0.001***	0.47(0.282, 0.782)	**0.004***
Residing at the roadside during pregnancy						
No	131	125	Ref			
Yes	51	32	0.658(0.397, 1.09)	0.104	0.933(0.536, 1.625)	0.808

OR = Odds Ratio and CI = confidence interval, * Statistical significance.

Correlation between maternal stress and psychosocial skills of infants

Majority (53.1%) of the respondents had no stress before pregnancy and among the stressors, financial worries such as food, shelter and transportation accounted for 36.9% cumulatively compared to other stressors followed by sleeping difficulties and other psychosomatic symptoms (26.8%). The least stressful was about problems related to current or previous pregnancy in which 92.9% of respondents indicated no stress followed by "having to move or change of settlements, either recently or in the future" (91.7%).

As to the level of stress among respondents during pregnancy, the analysis showed that 44.2% of the participants had stress during pregnancy which is lower compared to before pregnancy. Sleeping difficulties and other psychosomatic symptoms and financial worries like food, shelter, and transportation are the major stressors during pregnancy.

There was a negative correlation between maternal stress before pregnancy and psychosocial skills of offspring (r= -142, p=0.009). Also, there was a negative correlation between maternal stress during pregnancy and psychosocial skills of offspring (r= -147, p=0.007) (Table 5)

Table 5. correlation between maternal stress and psychosocial skills of offspring (n=339).

		Overall psychosocial profile of offspring	Maternal stress before pregnancy	Maternal stress during pregnancy
Overall psychosocial profile of offspring	r			
	p-value			
Maternal stress before pregnancy	r	-.142**		
	p-value	*0.009*		
Maternal stress during pregnancy	r	-.147**	.755**	
	p-value	***0.007***	***0.001***	

There was no correlation between the age of the mothers and psychosocial skills of infants (r=0.007, p=897).

Nutritional status of mothers against psychosocial skills of offspring

Supplements and vaccines are very important in the prevention and control of maternal diseases and conditions. In this study majority of the participants received tetanus toxoid (69%), 65.5% received iron supplementation and 71.4% received fansidar. However, majority of the respondents did not receive zinc supplementation (65.5%) and antibiotic prophylaxis (54.6%). More than half (51.9%) of the respondents acknowledged the use of excess nutrients before or during pregnancy. Also, 66.4% do take low protein diet, 84.4% also use high-fat diet.

The logistics binary regression analysis was conducted to determine possible predictors of the outcome variable (psychosocial skills). Mother who consumed low protein diet were almost three more likely to have infants with good psychosocial skills (OR=2.545, 95% CI: 1.529-4.237) (Table 6).

Table 6. Nutritional status as predictors of psychosocial skills of offspring (n=339).

Question	B	Wald	Sig.	OR	95% C.I	
					Lower	Upper
Excess nutrient intake	-0.084	0.129	0.72	0.92	0.583	1.452
High-protein diet (meat, fish, milk)	0.934	12.911	**0.001***	**2.545**	1.529	4.237
High-fat diet (butter, fries, cookies)	0.18	0.291	0.589	1.197	0.622	2.304

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Vegetable oil	0.209	0.301	0.583	1.233	0.584	2.602
Red meat	0.718	3.877	**0.049***	**2.05**	1.003	4.19
Dietary fiber (raw fruits, vegetables)	0.138	0.04	0.841	1.148	0.300	4.393
Rich vitamin foods (fruits, vegetables)	0.812	1.678	0.195	2.252	0.659	7.688
Taking supplements (e.g. vitamin)	0.106	0.185	0.667	1.112	0.686	1.801
Fasting	0.288	1.089	0.297	1.333	0.777	2.288

OR = Odds Ratio and CI = confidence interval, * Statistical significance.

Discussion

Globally, in addition to adult obesity, childhood obesity has reached epidemic proportions. This trend is not only affecting physical health but also far-reaching and economic implications. While some healthy lifestyle interventions can mitigate these serious metabolic disorders, there seems to be a race between these interventions and the passing down these deleterious traits to the next generation through epigenetic changes. Furthermore, epigenetic changes have similar consequences on intergenerational and transgenerational changes in brain function of the offspring. While much attention is paid to maternal epigenetic effects during gestation, paternal effects are as well phenomenal [16]. What lies the illusion is the biological processes with negative effects of trauma across generations, thereby identifying risk groups in intergenerational transmission of mental disorders and sorts [39]. Elucidating these occurrences in the population base will provide a clue to the biological mechanistic pathways as useful tools for their prevention [31, 32].

Neonatal complications can pose serious threats to the survival of the infant especially in the first 100 days. Our findings showed that a good number of the infants had poor suckling, fever, breathing problems and low birth weight. In addition to the episodes of infectious diseases common during the rainy season, the most extended endurance of eating the previous harvest when food stocks are depleted avails a chronically marginal diet. Previous study conducted in Gambia showed an increased death rate of individuals born in nutritionally poor seasons and this has been related to infections [3]. Reproductive women tend to lose weight (3–6 kg) due to the burden of laborious seasonal farm work. These seasonal average weights for pregnant women are better during the harvest season [17, 18]. This reduced weight leads to lower birth weight in infants born during the hunger season as compared to those born during harvest seasons [19, 20, 21]. From this study, we found that majority of the infants had good health record. However, a considerable number had low hemoglobin and asthma, and few had sickle cell disease. Despite the fact that most of the respondents' offspring had good social skills, some were found to fall under good social skills and almost the same proportions hold for communication and cognitive skills. Furthermore, a good number of offspring were found with a good motors skills activities of daily living.

Exposure to chemicals by parents especially the mother can predispose the infant or fetus to some medical complication. More than half of our study respondents were exposed to insecticides, DDT, mosquito spray or coil and even a greater number were found to be exposed to heterocyclicamines and to aflatoxin during the course of the pregnancy. Cypermethrin insecticide exposure was found to be correlated with a long-lasting reproductive malfunctions in female mice generations. Up to F2 generation of female line, developmental abnormalities were observed and this calls for a divergency to the molecular mechanism studies on trans-generational sex-linked [28]. In addition, a good number reside by the roadside, where they will be exposed to smokes coming from exhaust engine. Even a low dose of lead or Polybrominated diphenyl ethers/ lead mixture exposure was seen with behaviour repetitive patterns, and learning challenges in male mice. Moreover, systemic inflammatory response was also synergistic [30]. From our study, there was no association between smoking habit of parents and the psychosocial skills of their offspring. However, parents or fathers who worked in industrial areas were more likely to have offspring with poor psychosocial skills.

Although the pathophysiological pathway that could shed some light on the association between maternal stressors and offspring's neuropsychiatric illness is not fully elucidated, there is evidence from epidemiological and animal models in addition to infection

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and maternal overnutrition. Maternal psycho psychiatric stress puts the offspring at an increased neuropsychiatric risk [25]. At least more than half of the respondents had no stress before pregnancy. However, among the stressors, financial worries such as food, shelter and transportation accounted for one third, then sleeping difficulties and other psychosomatic symptoms. The least stressful was about problems related to current or previous pregnancy in which almost all the respondents indicated no stress and also "having to move or change of settlements, either recently or in the future" was not a big problem among the respondents. It is obvious that the kind of prenatal maternal stress, exposure timing could determine the infant immune epigenetic profiles [43]. There was a statistical significance between paternal early life stress (ELS) and the development of offspring's brain development. Thus, there is a need to expand pediatrics studies on intergenerational inheritance of ELS on generations related brain development [38]. Prenatal stress alters metabolic pathways in protein and energy metabolism and these are predictive of an increased risk of insulin resistance, obesity and diabetes [33]. A good number of our study respondents had an increased stress during pregnancy. These could be caused by sleeping difficulties and other psychosomatic symptoms. In addition, financial worries like food, shelter, and transportation were the major stressors during pregnancy. From our study findings, we could detect a negative correlation between maternal stress before pregnancy or during pregnancy and psychosocial skills of offspring. In contrast to our study findings, at 16 months after birth, the infants were seen with lower fine motor development and difficult temperament. However, the same study could not find any association between infant salivary cortisol and prenatal maternal distress [45]. In predicting the factors associated with psychosocial skills from our study, mothers who are exposed to oxidative stress and high temperature are more likely to have offspring with poor psychosocial skills.

Supplements and vaccines are very important in the prevention and control of maternal diseases and conditions. Acetaminophen or paracetamol as one of the common medicines taken during pregnancy has epidemiological background its association with risk for neurodevelopmental disorders, asthma, genital malfunctions and behavioral changes in offspring [29]. In this study majority of the participants received tetanus toxoid, iron supplementation and fansidar. However, majority of the respondents did not receive zinc supplementation and antibiotic prophylaxis. Moreover, maternal zinc status did not influence developmental outcomes in children as previously thought with central nervous system development [31]. Like other middle-income countries, there are seasonal nutritional fluctuations. This substantial phenomenon is experienced naturally in some rural farming communities. Studies found this to be causing maternal undernutrition, especially during prolonged dry periods locally called 'hungry season' in Gambia [13]. Eating disorders are associated with increased risk of adverse outcomes such as preterm delivery, miscarriage, poor fetal growth, or malformations [42]. Immune dysfunction in autistic offspring via superoxide dismutase 2 suppression is found to be induced by maternal diabetes [36]. Maternal diabetes induced neurodevelopmental disorder like autism-related phenotypes in offspring is potentiated by vitamin D deficiency [40]. In this study, more than half of the respondents acknowledged the use of excess nutrients before or during pregnancy, high protein diet, and use high-fat diet. Mother who consumed high protein diet were almost three more likely to have infants with good psychosocial skills.

Although the study involved the mothers by going through the antenatal card to read through the ANC while ascertaining some medical history, the level of literacy and health education among mothers in Gambia is relatively low. This has serious implications on the credibility of some information and how representative the sample size might be. To explore intergenerational effects of gestational nutrient restriction and its effect on the population, it will require decades to make a follow up study. Furthermore, to meet the reliable disease history, it requires data, which is very limited. In response to this, follow-up study or retrospective becomes very necessary. While this study is an observational study, there was no enough fund that could enable an increased sample size to overcome the biases in sampling and responses. Epidemiological evidence, instead of genetic data,

is added in the scientific literature. Despite the fact that well experienced community nurses break down questionnaires through home visit interviews, due to high illiteracy rate, some participants were not able to recall or identify specific cardiometabolic diseases.

This emerging paradigm shift in science on epigenetic modifications has a permanent imprint on phenotypic responses [44]. It is obvious that nutrition, stress status and parental metabolic conditions altered epigenetic intergenerational transmission. While this is trending, we strongly recommend policy implications that will reduce the continuous disadvantages across the generations. This will no doubt check the insights of the perpetuation of compromised lives across generations. With a larger sample size study, a well design structured intervention could be established during every stage of pregnancy and also during the postpartum period. While addressing diets seem more feasible as compared to developing new pharmacological targets, dietary monitoring connects physiological pathways in the complex human body with positive effects and can check metabolic as well as mental disorders. It is prominent to include primary lifestyle changes among reproductive-age women, which should be on dietary selections and also switching dietary options during nutrition restrictions times. Furthermore, there should be an increased level of awareness of mothers on their offspring health being and their husbands' lifestyles that might influence the adulthood health of offspring.

Conclusions

The developmental origin of the health of young adults got its basis on the socioeconomic disadvantages and maternal prenatal distress. This affects both short and long term mental and physical health of the offspring. However, the biological system involved in the transmission of these factors across the generations is not fully documented due to the utero timeframe. While the epigenetic pathways of parental childhood experiences of these phenomena are only beginning to be studied in humans, translational research with a viewpoint on human cohort studies based on solid study design and valid methodological approaches combined with the existing longitudinal studies should be considered. This study provided evidence base findings on the influence of parental energy, toxicant exposure, age and nutrient restriction on offspring growth in Gambia. The study was able ascertain if maternal diet during gestation, toxicant exposure, maternal stress and parental smoking habits have influence the early life of offspring.

Abbreviations: aOR-adjusted Odds Ratio; ANC-annenetal calls; CKD-chronic kidney disease; CI-Confidence Interval; ELS-early life stress; SPSS-Statistical Package for Social Sciences

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Supplementary Table 1 Socio-demographic characteristics of the participants (n = 339)

Variable	Category	Frequency	Percentage
Region of Origin			
	Central River Region	14	4.1
	Upper River Region	7	2.1
	Lower River Region	16	4.7
	North Bank	42	12.4
	Banjul	9	2.7
	Western Region	182	53.7
	Kanifing Municipality Council	56	16.5
	Foreigners	13	3.8
Child alive or not			
	Alive	335	98.8
	Dead	4	1.2
Sex of child			
	Male	173	51
	Female	166	49
Marital status			
	Married	313	92.3
	Divorced	7	2.1
	Single	16	4.7
	Widow	3	0.9
Occupation of mother			
	Housewife	245	72.3
	Civil servant	38	11.2
	Farmer	6	1.8
	Self-employed	38	11.2
	Others	12	3.5
Occupation of father			
	Civil servant	212	62.5
	Farmer	28	8.3
	Construction worker	46	13.6
	Not employed	53	15.6
Residence of participant			
	Municipality regulatory area	265	78.2
	Moderate municipality regulatory area	41	12.1
	Non-municipality regulatory area	33	9.7
Settlement type			
	Urban	312	92
	Rural	27	8
Type of bathrooms			
	In house bathroom	192	56.6
	A short distance behind house	143	42.2
	Far from the house (public)	4	1.2
Highest Education completed			
	Primary	82	24.2
	Secondary	136	40.1
	Tertiary	59	17.4
	No education	62	18.3
Cooking			
	No	10	2.9
	Yes	329	97.1

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Cleaning			
	No	9	2.7
	Yes	330	97.3
Laundering			
	No	17	5
	Yes	322	95