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Approaching a Dysmorphic Newborn

Sahar M Nour El-Din[1], Maisa N Farid[2], Ahmad Ramy M Ramy[3]

[1]Medical Genetics Center, [2]Institute of Postgraduate Childhood Studies; [3]Obstetric and Gynecologic Department, Ain Shams University

ABSTRACT

Background: Dysmorphology combines concepts, knowledge and techniques from field of embryology, clinical genetics and pediatrics. It deals with people who have congenital abnormalities and their families. Clinical delineation of dysmorphism and dysmorphic syndromes is crucial for patient management and family counseling.

Patients and Method: Forty case mothers and neonates, 83 control mothers and neonates were recruited in the study. Face to face interviews were conducted with the mothers of both cases and controls. Case's mothers and neonates were subjected to certain investigations according to dysmorphic anomaly and when needed.

Results: The study showed that increased risk of having a dysmorphic child was associated with high consumption of legumes and the use of kerosene in cooking stoves. Their Odd Ratio (OR) and Confidence Interval (CI) respectively were [OR=15558.0; CI 137.0-17716.2] and [OR=186.7; CI 42.3-824.5]. Maternal demographic risk factors were, medication intake (OR=29.62; CI 3.38-112.5), diseases during pregnancy (OR=24.13; CI 5.92-114.18), maternal occupation (OR=15.4; CI 1.78-132.8), and educational attainment (OR=2.85; CI 1.19-6.86). In rural areas the rate of having dysmorphic child is higher than that in urban areas (OR=11.85; CI 3.60-38.99), (p-value=0.00). Consanguinity (OR=4.35; CI 1.927-9.796), was a key risk factor contributing to dysmorphology. Drinking water which is obtained by pumps was significant in this study (OR=27.3; CI 3.4-222.7) as well as ghee consumption (OR=6.3; CI 2.4-16.4).

Conclusion: In conclusion, the considerable challenge posed by dysmorphic abnormalities calls for the development of prevention programs through the establishment of community genetic services particularly those related to maternal education and environmental exposures. These primary prevention measures should be integrated into primary health care.

Key Words:

Dysmorphology, morphogenesis, dysmorphic syndromes, teratology, ecogenetics.

Corresponding Author:

Sahar Nour El-Din
E-mail: sahar-gen79@yahoo.com

INTRODUCTION

Dysmorphology is the professional discipline of delineating disorders affecting the physical development of the individual, before or after birth.

It includes recognition of specific patterns of physical features in patients with a range of problems; sometimes including delayed intellectual development. Patients are mainly babies, children and teenagers or young adults. Genetic services are involved because the majority of these syndromes have a genetic basis. The two main genetic bases are: (i single gene defect and ii) chromosomal abnormalities. In many cases these are spontaneous events; in some cases they may be inherited, familial conditions. Over 3.000 conditions and syndromes have been described.[1]

The work of the genetic services includes the ascription of specific conditions to patients. This involves the assembly of a clinical description, including the characterization of the patient's physical appearance, including–but not exclusively–the appearance of the head and face. Clinicians decide whether appearances are normal or abnormal, and if abnormal whether they correspond to a dysmorphic clinical entity.[2]

There is now a number of laboratory tests that can be applied in the investigation of possible dysmorphic conditions, including DNA and chromosomal testing. It is not the case, however, that these molecular and cytological tests supplant the expertise of clinical description, inference and classification.[3]

Appropriate tests are ordered in the light of clinical decisions and differential diagnosis. The relationship between phenotype (Manifestations of the patient's condition) and the genotype (The underlying DNA or chromosomal anomaly) is not entirely predictable. Sometimes molecular evidence does not conform to the clinical adjudication and attribution of syndromes. Laboratory tests do not, however outweigh clinical evidence.[4]

Reaching an accurate diagnosis for children with dysmorphic signs is important to their families, because it makes available all the accumulated knowledge about the relevant condition and may provide the family with the opportunity for interaction with the patient.[5]

AIM OF THE STUDY

The aim of this study was to estimate the risk factors which may predispose to dysmorphism in newborns in Egypt.

PATIENTS AND METHODS

This case-control study included cases that were recruited from maternity out patient clinic in Human Genetics Unit (HGU), at Ain-Shams University.

The controls were also recruited from maternity hospital at Ain-Shams University. This hospital is a referral hospital that serves both urban and rural areas. Time of recruitment of subjects was between the years 2005-2007.

Subjects:
Cases: They included 40 newly born babies with apparently dysmorphic features and their respective mothers.

All newborns with dysmorphic features were either diagnosed prenatelly (Through obstetric ultrasonography) or diagnosed after delivery.

Controls: This group included 83 apparently healthy looking newly born babies and their respective mothers, they were matched with age, parity and social class, to those of dysmorphic neonates, and they were subjected to the same procedures and questionnaire completion as cases.

Inclusion criteria:

Cases:

- Dysmorphic neonate.
- Stillbirth, died within one week (Or alive till one week).

Controls:

- Apparently healthy neonates.

Exclusion criteria:

Cases:

All apparently healthy looking newly born and their mothers were excluded.

- Any normal child coming with the parents for counseling.
- Any neonate more than one week of age.

Controls:

- Any neonate with birth defect whether major or minor abnormality.
- Neonates suffering from any disease or from complication after birth.

Methods:

All newborn were subjected to the following:

1. Thorough clinical examination laying stress on the physical examination including:
    - General appearance (Built, facial features).
    - Measurements (Weight, length).
    - Head (Head circumference, skull shape).
    - Eyes (Sun-set appearance, blue sclera, xerosis).
    - Nose (Depressed nasal bridge, saddle shape).
    - Mouth and oral cavity.
    - Ears (Low set ears, small ears).
    - Neck (Short neck, webbing, masses).
    - Extremities (Short, deformed).
    - Chest and abdominal wall.
    - Spine (Spina bifida).

2. Further investigations were done e.g. radiological examination (X-ray, ultrasound), chromosomal studies or biochemical and other laboratory evaluation to identify the possible underlying pathology.

3. All parents of cases had a karyotype which was normal for mothers (46, XX) and fathers (46, XY).

4. The mothers of dysmorphic newborns were interviewed and a predefined questionnaire was designed as guided by Gillham et al.[6]

The questionnaire was phrased in English and was translated verbally into Arabic. Some paternal exposures were also included in the questionnaire.

N.B. Socio-economic status was classified based on a grading of occupations according to their level of skill and financial rewards, and on the general status they confer in the community.

In this classification there are five classes:

Class 1: Highest income. Jobs requiring higher education, e.g. doctors, headmasters, company directors, senior civil servants.

Class 2: Skilled occupations requiring secondary education, e.g. school teachers, technicians, nursing sisters, officers in police, army or prison service.

Class 3: Occupations requiring upper primary or lower secondary education, e.g. clerks, post office workers, auxiliary nurses, drivers, machine operators, painters, mechanics.

Class 4: Occupations requiring primary education at lower level only, and for which suits or uniforms are usually worn, e.g. messengers, shop assistants, waiters.

Class 5: Lowest income. No education or formal training required, e.g. gardeners, labourers, street cleaners.

Obstacles of the study:
Completing the questionnaire during interviews was a very daunting task. There are many communication difficulties particularly with illiterate mothers. Some mothers tended to flood the Enquirer with a flux of information on things they imagined to be the reason behind having their dysmorphic children.

Statistical analysis:
Package used was SPSS version II software, the data of questionnaire were installed in the computer by coding every data of the variable to make it easier to calculate, then interpreting and analyzing the output.

Quantitative variable, e.g., age, are expressed as the mean and standard deviation (SD) and compared by t-test.

Qualitative variables, e.g., sex, are expressed as proportion. Cross tabulation was done between qualitative variables and quantitative variables. Quantitative variables changed to the appropriate categories using the suitable cut-off points. Testing the significance of the association was done by the Chi-square test (X^2), while odds ratio was used to measure the association and the precision of the odd (OR) was assessed by confidence interval (CI). A critical value of 0.05 was set for the significance level or the p-value.

RESULTS

Table 1: A total of 40 cases (Neonates) with the following dysmorphic features identified during the study period.

Dysmorphic features	Frequency	Percentage (%)
Hydrocephalus	7	17.5%
Microcephally	7	17.5%
Achondroplasia	6	15%
Anencephaly	4	10%
Multiple deformities	3	7.5%
Osteogenesis imperfecta	3	7.5%
Down syndrome	3	7.5%
Cleft lip and palate	3	7.5%
Bone deformity	1	2.5%
Blindness	1	2.5%
Sanjad-Sakatti syndrome	1	2.5%
Anal atresia	1	2.5%
Total	**40**	**100%**

Table 2: Sex distribution among cases and controls.

Cases		
Sex	**No.**	**%**
Male	27	67.5%
Female	13	32.5%
Total	**40**	**100%**
Controls		
Sex	**No.**	**%**
Male	51	61%
Female	32	39%
Total	**83**	**100%**

Table 3: Maternal and paternal age in cases and controls.

Variable	Cases (n=40) Mean (SD)	Controls (n=83) Mean (SD)	Sign. (t-test)
Maternal age (years)	25.68 (4.65)	28.1 (6.2)	Sign.
Paternal age (years)	31.55 (5.7)	34.0 (6.69)	Sign.
Marital age (for mothers [years])	19.6 (5.52)	18.82 (4.7%)	Not sign.

Table 4: Demographic characteristics of cases and control parents.

Variable	Case n=40	Control n = 83	Odd Ratio (CI)	X^2	p-value
Residence					
- Urban	25 (62.5%)	79 (92.2%)	11.85 (3.60-38.99)	22.072	0.000*
- Rural	15 (37.5%)	4 (4.8%)			
Land marks *					
No.	7 (17.5%)	15 (18.1%)	1.04 (0.387–2.795)	0.06	0.938
Yes	33 (82.5%)	68 (81.9%)			
Socio-economic level					
- Social class 2,3 (Teachers, shopkeepers, skilled non-manual workers	17 (42.5%)	17 (20.5%)	2.87 (1.17-7.10)	6.49	0.010*
- Social class 4,5 (Partly skilled workers, unskilled workers)	23 (57.5%)	66 (79.5%)			

* ***Land marks:*** Parents living in areas with e.g. high voltage electric power stations, hospitals, industrial and manufacturing areas, car maintenance and repair area, garbage collecting areas, military bases and agricultural lands, telecommunication centers.

Table 5: Comparison between cases and controls as regard paternal and maternal risk factors for dysmorphic neonate.

Variable	Case n = 40	Control n = 83	Odd Ratio (CI)	X²	p-value
Paternal Factors:					
Paternal age					
- Less than 40 years	36 (90%)	64 (77.1%)		2.951	0.141
- At risk 40 or more	4 (10%)	19 (22.9%)			
Paternal occupation					
- Labourers	27 (67.5%)	65 (78.3%)	0.58 (0.23-1.45)	1.96	2.247
- Civil servants	13 (32.5%)	18 (21.7%)			
Duration of occupation exposure (e.g. exposure for solvents, and agricultural chemicals).					
- Short duration	28 (70%)	82 (98.8%)	35.14 (4.37-282.6)	23.678	0.001*
- Long duration	12 (30%)	1 (1.2%)			
Paternal educational level					
- Educated (university, diploma, high school degree)	21 (52.5%)	30 (36.1%)	0.512 (0.80-4.32)	2.5	0.112
- Non-educated (read and write, illiterate)	19 (47.5%)	53 (63.8%)			
Maternal Factors:					
Maternal age					
- Mid reproductive years	37 (92.5%)	60 (72.3%)	0.212 (0.059-0.75)	6.614	0.025*
- Less than 20 more than 35 years	3 (7.5%)	23 (27.7%)			
Maternal occupation					
- Non	32 (80%)	82 (98.8%)	15.4 (1.78-132.8)	14.060	0.0001**
- Other Jobs	8 (20%)	1 (1.2%)			
Consanguinity					
- Non-consanguineous	12 (30%)	54 (65.1%)	4.35 (1.927-9.796)	13.343	0.000*
- Consanguineous	28 (70%)	29 (34.9%)			
Maternal educational level					
- Educated (university, diploma, high school degree)	19 (47.5%)	20 (47.5%)	2.85 (1.19-6.86)	6.83	0.0089*
- Non-educated (read and write, illiterate)	21 (52.5%)	63 (75.9%)			

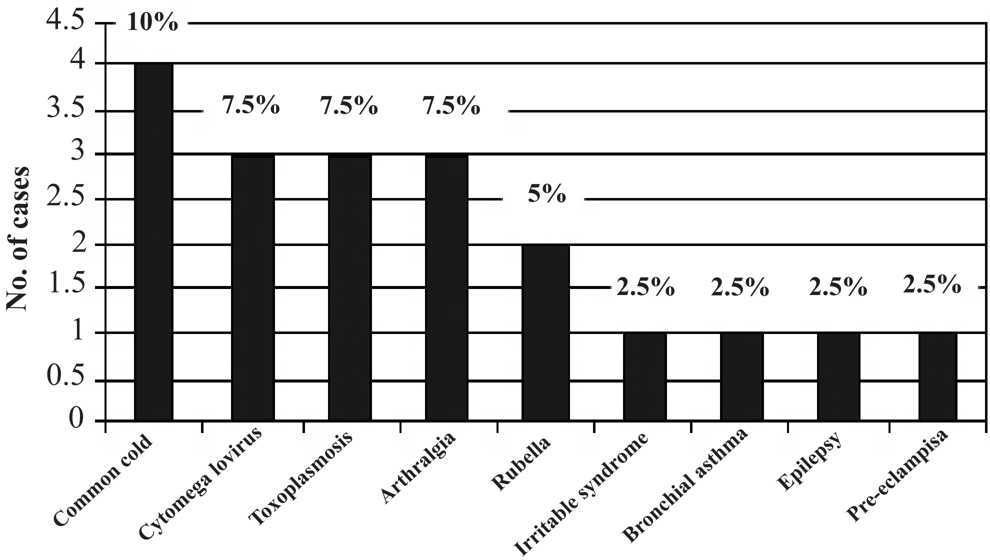

Fig. 1: Medical disorders reported by mothers of cases during the index pregnancy, which represents 47.5% of index cases (19/40 cases)

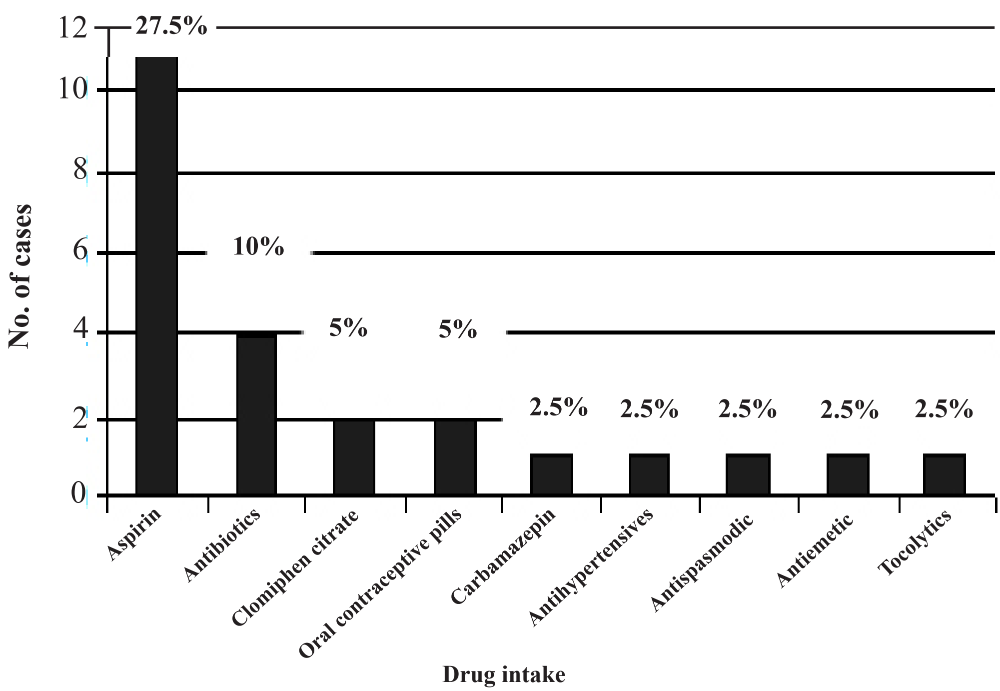

Fig. 2: History of drug intake during the index pregnancy in 40 case mothers, which represents 60% of index cases (24/40 cases).

Table 6: Household facilities evaluated in determination of risk factors for dysmorphic neonate.

Variable	Case n = 40	Control n = 83	Odd Ratio (CI)	X^2	p-value
House Hold detergent					
- No	14 (35%)	48 (57.8%)	2.55 (1.17-5.57)	5.628	0.02*
- Yes	26 (65%)	35 (42.2%)			
Insecticide use					
- No	16 (40%)	54 (65.1%)	2.79 (1.28-6.88)	6.913	0.011*
- Yes	24 (60%)	29 (34.1%)			
Aluminium use					
- No	1 (2.5%)	0 (0%)	-	2.092	0.3
- Yes	39 (97.5%)	83 (100%)			
Teflon use					
- No	38 (95%)	80 (96.4%)	1.40 (0.23-8.76)	0.133	1.0
- Yes	2 (5%)	3 (3.6%)			
Enamel use*					
- No	36 (90%)	82 (98.8%)	9.11 (0.99-84.40)	5.354	0.038*
- Yes	4 (10%)	1 (1.2%)			
Butagas use					
- No	7 (17.5%)	4 (4.9%)	0.24 (0.07-0.88)	5.330	0.03*
- Yes	33 (82.5%)	79 (95.1%)			
Kerosene stoves (primus gas)					
- No	5 (12.5%)	80 (96.4%)	186.7 (42.3-824.5)	88.964	0.000*
- Yes	35 (87.5%)	3 (3.6%)			
Farmer oven					
- No	35 (87.5%)	82 (98.9%)	11.71 (1.32-103.96)	7.422	0.014*
- Yes	5 (12.5%)	1 (1.2%)			
Natural gas use					
- No	35 (87.5%)	82 (98.9%)	11.71 (1.32-103.96)	7.422	0.014*
- Yes	5 (12.5%)	1 (1.2%)			

* Utensils glazed with heavy metals such as mercury, lead oxide and arsenic

Table 7: Comparison between mothers of cases and controls during conception as regard dietary factors and type of drinking water sources.

Variable	Case n = 40	Control n = 83	Odd Ratio (CI)	X^2	p-value
Using fresh vegetables					
- No	1 (2.5%)	7 (8.33%)	3.59 (0.43-30.24)	1.563	0.27
- Yes	39 (97.5%)	76 (91.57%)			
Legume consumption/day					
- No	2 (5%)	1 (1.2%)	1558.0 (137.0-17716.2)	109.663	0.000**
- Yes	38 (95%)	82 (98.8%)			
Eating beef /week					
- No	8 (20%)	42 (50.6%)	4.1 (1.69-9.94)	10.478	0.25
- Yes	32 (80%)	41 (49.4%)			
Eating lamb / week					
- No	38 (95%)	82 (98.8%)	4.32 (0.38-49.1)	1.634	0.000**
- Yes	2 (5%)	1 (1.2%)			
Eating poultry / week					
- No	26 (65%)	15 (18.1%)	0.12 (0.50– 0.28)	26.749	0.000**
- Yes	14 (35%)	68 (81.9%)			
Eating fish / week					
- No	23 (57.5%)	15 (18.1%)	0.17 (0.07 – 0.38)	19.654	0.000**
- Yes	17 (42.5%)	68 (81.9%)			
Using butter					
- No	38 (95%)	79 (95.2%)	1.04 (0.182-5.928)	0.002	1.0
- Yes	2 (5%)	4 (4.8%)			
Using "Ghee"					
- No	24 (60%)	75 (90.4%)	6.3 (2.4-16.4)	15.843	0.000**
- Yes	16 (40%)	8 (9.6%)			
Using vegetable oils					
- No	28 (70%)	48 (57.8%)	0.59 (0.263-1.314)	1.693	0.24
- Yes	12 (30%)	35 (42.2%)			
Drinking from pipe lines					
- No	0 (0%)	3 (3.6%)	-	1.482	0.55
- Yes	40 (100%)	80 (96.4%)			
Mineral water					
- No	40 (100%)	82 (98.8%)	-	0.486	1.0
- Yes	0 (0%)	1 (1.2%)			
Sources of water					
Wells					
- No	39 (97.5%)	82 (98.8%)	2.1 (0.13-34.5)	0.283	1.0
- Long duration	1 (2.5%)	1 (1.2%)			
Water pumps					
- No	30 (75%)	82 (98.8%)	27.3 (3.4-222.7)	18.768	0.000**
- Yes	10 (25%)	1 (1.2%)			

Table 8: The prevalence of the most important risk factors among mothers having dysmorphic neonate.

Risk factor	OR	CI
Daily legumes consumption	1558.0	137.0-17716.2
Kerosene for cooking	186.7	42.3-824.5
Duration of father's occupation	35.14	4.37-282.6
Medications intake	29.62	9.04-97.1
Diseases during pregnancy	29.47	7.96-109.13
Water pump	27.3	3.4-222.7
Maternal occupation	15.4	1.78-132.8
Rural residence	11.85	3.60-38.99
Hair dying	11.76	2.41-57.50
Farmer's oven natural gas	11.71	1.32-103.96
Enamel use	9.11	0.99-84.40
Ghee consumption	6.3	2.4-16.4
Consanguinity	4.35	1.927-9.79

DISCUSSION

Dysmorphology is a relatively modern science which is very wide and continuously advancing.[7] It is described to be the medical study of abnormal forms in the humans. Also, it is described as an art.[8]

Approximately 2400 dysmorphic syndromes are described that are believed to be due to molecular pathology in single genes, and for about 500 the genes have been identified and a further 200 or 29 mapped. A further 500 or 50 sporadically occurring syndromes are recognized, for which the precise cause remains elusive.[9]

Having a dysmorphic newborn is a situation of parental concern. Parents are usually concerned about the causes behind such dysmorphic appearance, the prospects of physical and mental development of such a child and of course the chances of this condition affecting future offspring.[10]

In the current study, some maternal risk factors appear to be associated with birth defects. A lower social class was associated with a greater risk of abnormal perinatal outcome. As the study was at a referral university hospital, most mothers were from moderate to low social class, and so the quality of prenatal care is not good. Also, prenatal nutrition is not adequate increasing their risk for having offspring with structural anomalies as neural tube defects.[11]

In accordance with the current study, a study published by Vrijheid et al.[12], showed that the more socio-economic deprivation the higher the risk of certain congenital anomalies of non-chromosomal origin such as all cardiac defects, malformations of the digestive system and multiple malformations. Thus, risk factors which could mediate the impact of socio-economic status on the prevalence of congenital anomalies, include nutritional factors, life style, environmental and occupational exposures, access to and use of health services, parity and maternal age.

Also, Farley et al.[13], reported association between low socio-economic status and the risk of awareness of the potential benefit of folic acid supplements in preventing neural tube defects.

In the present study, the maternal age had a relationship with birth defect in which the mid-reproductive age showed to have more dysmorphic children than the mothers in the extremes of reproductive years.

In accordance to this study, Ales et al.[14], concluded that advanced maternal age was not associated with an excess of adverse pregnancy outcome and suggested that with early registration and careful surveillance during pregnancy, women aged 35 years or more can experience excellent pregnancy outcome.

However, another study published by Reefhuis and Honein[15] showed that young and advanced maternal ages was associated with different types of birth defects.

Also, Vieira and Castillo[16], found an increased risk of having an offspring with neural tube defects (*Spina bifida*) for mothers 40 years of age or older and mothers 19 years or younger.

The maternal occupation in this study appeared to be a risk factor for having a dysmorphic child, OR=15.4; CI (1.78-132.8), p=0.0001.

Of note, in the current study, there were two mothers (5%) working as nurses at heamodialysis unit for seven and eight years, respectively, before giving birth to their dysmorphic children. This was similar to a study done by Matte et al.[17], which showed that offspring of mothers employed in a nursing occupation during the periconceptional period had a modest excess risk of having at least one congenital defect such as anencephally or spina bifida. The rest of cases in this study were non-working (80%) most of these mothers came from rural areas to the referral hospital, and many gave help to their husbands in the farms and agricultural lands, so they could have been potentially exposed to pesticides.

Shawky et al.[18], reported that maternal exposure to pesticides leads to selected congenital anomalies such as orofacial clefts, neural tube defects and limb anomalies.

A recent study reported that there were no association between persistent organochlorine pesticides and adverse birth outcomes in contaminated mothers.[19]

In the current study, maternal education showed an association with having a dysmorphic child, p value=0.0089; OR=2.85; CI (1.19-6.86).

This could be explained by a study which was done by Robinson et al.[20], and reported strong association between better education and compliance with healthy or prudent eating.

Another study done by Van der et al.[21], published that education had such a marked effect on the food choices of women with low or no educational attainment leading to poor quality of food, low fruit and vegetable consumption resulting in less favourable profile of biomarkers, including plasma folate and raised homocysteine levels which leads to neural tube defects.[22]

In the present study (60%) mothers of dysmorphic babies reported medications intake such as warfarin, aspirin, antibiotics, contraceptive pills, clomid, and carbamazepine. There was a highly significant (p-value=0.000) association of medications intake during pregnancy and having a dysmorphic child, (OR=29.62; CI (9.04-97.1). It could not be defined if this association was related to drug intake itself or to maternal medical condition requiring the intake of the medication.

Many studies[23,24,25] showed that medication intake during pregnancy was a risk factor for having a dysmorphic child, some of these medications were, antiepileptic drugs, carbamazepine[26], aspirin[27] and warfarin.[28]

Consanguinity in this study was a risk factor for having a dysmorphic child, most of these cases were first cousin marriages, OR=4.35; CI (1.93-9.8).

This was consistent with a study done by Meguid et al.[29], in Egypt, which showed that consanguinity was an important risk factor in the causation of birth defects.

Also, Temtamy et al.[30], described that birth defects in the offspring of first cousin parents were higher than in the offspring of non-consanguineous parents in Egypt.

The present study revealed that the paternal occupation was not a risk factor for having a dysmorphic child, while the duration of paternal occupational exposure showed an association, (OR=35.14; CI (4.37-282.6), p-value=0.001.

However, a study done by Chia et al.[31], reported that the common paternal occupations associated with birth defects were, painters, printers, and occupations exposed to solvents, fire fighters or firemen, and occupations related to agriculture similar to the present study. Several studies[32-33] explained the associations between duration of paternal exposures and congenital anomalies in offspring. Most congenital malformations (Neural tube defects) were thought to be due to the interaction of both environmental and genetic influences.

In the current study, as regards paternal ages (90%) of cases having dysmorphic children were less than 40 years old. However, Savitz and his Colleagues[34] found that advanced paternal age was associated with increased risk of preauricular cyst, nasal aplasia, hydrocephalus and hemiangioma. Spontaneous mutations in germ cells increase with male age and are induced by biological or environmental factors so advanced paternal age may be associated with an excess occurrence of some specific malformations of extremities and syndromes of multiple systems, as well as, Down's syndrome.[35]

Paternal education in this study, showed that university and high school graduates were more likely to have a dysmorphic child. This could due to more awareness and understanding of the conditions.[36]

In the current study, consumption of red meat (Beef and lamb) and legumes were associated with increased risk of having a dysmorphic child, while, consumption of poultry and fish were significant for not having a dysmorphic child. In addition, consumption of fresh vegetables and fruits did not appear to affect the risk. Modern agricultural and farming techniques have had the unwelcome effect of polluting meat with significant levels of dangerous toxins. Animals in modern industrial farms are routinely given growth hormone, antibiotics, toxic antitoxins, and pesticides. These chemicals remain in the animal's tissues and are transferred over to the human body upon consumption of the meat. Most of these chemicals have adverse effects ranging from causing birth defects to causing mutations.[37]

Secondly, the meat might be contaminated by toxoplasma gondii. Women caught toxoplasma infection by consumption of undercooked meat or tasting meat while preparing meal.[38]

In the present study, mothers of dysmorphic children showed significant tendency for less consumption of fish in their diet, which might be itself a risk factor for the development of dysmorphism or it can be a marker of other nutritional deficiencies.

Weisskopf et al.[39], reported that fish consumption may be beneficial for a developing human fetus.

This differ than Turkey et al.[40], study which showed that fish is a potential route of exposure for environmentally persistent organochlorine contaminants, so all major malformations were increased with having more than 2 meals of fish per month during pregnancy.

Legumes being a substantial and cheap source of dietary protein, a large scale of population depends on its daily consumption. In this study there were strong association between legume consumption and having a dysmorphic child. The explanation could be due to legumes storage contamination. In Egypt, most of the months of the year are characterized by high temperature and humidity which are favorable to the growth of mold; commonly mycotoxins "alfatoxins" which are not broken down or destroyed by cooking temperature. Alfatoxins are mutagenic, carcinogenic and teratogenic[41], and alfatoxins induce chromosome aberrations.[42]

In the current study the use of "natural animal fat" or ghee showed statistically significant association with having a dysmorphic child. This might be due to that most of mothers cases were coming from rural areas where they depend on the ghee extracted from the animals that they breed up.

In the current study living in rural areas was more strongly associated with having a dysmorphic child than living in urban areas. Living in rural areas is associated with lower education of parents, lower economic status and living near agricultural land with possible pesticide pollution. Also there is a tendency for extended large families to live in the same house, and the presence of farmer's oven (Fueled with wood, dung or crop residue) inside the house, with poor living conditions. Added to that is prevalence of consanguinity and couples tending to marry at very young age. Moreover, women living in rural areas may be at a disadvantage in accessing health care.

However, Perera et al.[43], published that the inner city population were at high risk for adverse birth outcomes due to exposure to environmental contaminants, including environmental tobacco smoke, polycyclic aromatic hydrocarbons (PAHS) and pesticides (*Organophosphorus* and *chlorpyirifos*).

Another study done by van Santen et al.[44], showed that the higher the degree of urbanisation, the higher the birth prevalence and fatality rate of malformed infants. Not only air pollution in urban areas but also over population can have an impact on reproductive outcomes.

The current study revealed an association between drinking water by using water pumps and an increased risk of having a dysmorphic child. Well water might be contaminated by chlorinated and aromatic solvents (Industrial toxic solvents mainly trichloroethylene and benzene). This group of contamination is known to induce congenital heart defects.[45] Bove et al.[46], reported that when chlorine disinfectant reacts with organic matter in the drinking water, it leads to the formation of trihalomethanes suspected to cause birth defects mainly central nervous system, cardiac and oral clefts.

In Egypt, the cooking fuels used, vary among different classes of people: neutral gas, propane gas cylinders, kerosene stoves and farmer's oven using wood, dung or crop residue.

In this study, household energy use showed an association with having a dysmorphic child. The most important of which was using kerosene as the risk was OR=186.7; CI (42.3-824.5).

Gilboa et al.[47], reported that smoke from burning fuels contain large quantities of carbon monoxide (Co) which bind with haemoglobin (HbCo), effectively reducing the amount of oxygen reaching the body tissues causing anemia. This is particularly important for women because they have less haemoglobin than men. In addition their natural levels of HbCo are greatly elevated during pregnancy. As women do most of the cooking and so they are the most exposed to (Co), it has been linked to reduced fetal growth, low birth weight and increased perinatal mortality.

In this study the use of insecticides showed a significant relation with having a dysmorphic neonate.

Khattak et al.[48], published that high levels of exposure to pesticides may contribute to birth defects; also, this study mentioned that certain pesticides such as polychlorinated biphenyls PCBS, have weak estrogen-like qualities called endocrine disrupters that may affect development of fetus reproductive system.

Enamel utensils usage in the present study showed an association of having a dysmorphic neonate (p-value=0.03).

The explanation might be that the enamel utensils used are of poor quality and are glazed with heavy metals such as mercury, lead oxide and arsenic.

The current study showed that mothers of dysmorphic neonates exposed to house hold detergents had two and half folds OR (2.55) increased chance of giving birth to a dysmorphic neonate than control mothers. This is supported by a study done by Shaw et al.[49], they reported that pesticides added to soap and household cleaning products cause orofacial cleft and neural tube defects.

Also, Chervrier et al.[50], reported that defects that occurred in babies born to women exposed to these chemicals as detergents (Mixture) included micropenis deafness, clubfoot, neural tube defects.

Another study done by Bay et al.[51], showed that maternal exposure to these chemicals (Endocrine disrupts) cause testicular dysgenesis syndrome (Cryptorchidism, hypospadias, impaired spermatogenesis and testis cancer).

The risk factors identified in this study may help other reaserchers to conduct additional aetiological studies and to establish more comprehensive strategies for the prevention of birth defects in Egypt.

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